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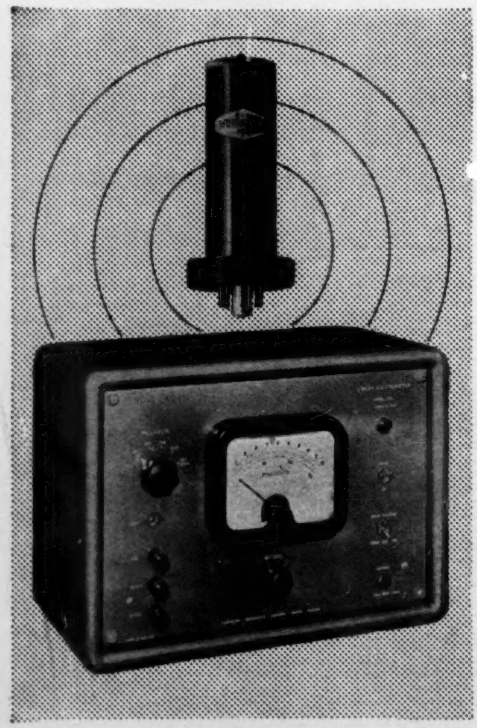

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INTERNATIONAL CO-OPERATION IN SCIENTIFIC RESEARCH

THE address in which the Right Hon. R. C. Casey, the Minister for External Affairs and Minister in Charge of the Commonwealth Scientific and Industrial Research Organization, Australia, asked the General Assembly of the United Nations, on September 25, to make more concerted world action to stimulate scientific research for the welfare of mankind a priority task of the Economic and Social Council in 1959 has strong claims on the attention of both scientists and technologists. Mr. Casey was particularly concerned with the time-lag between scientific discoveries and their application to production and human welfare; but he began with a reference to the International Geophysical Year and to the value of the artificial Earth satellites, not only as a spectacular advance in technology but also as a potential source of new scientific data about the regions of space immediately surrounding our planet. Australia has taken full advantage of its special opportunities for research in optical and radio-astronomy which arose from its situation in the southern hemisphere, and her scientists have co-operated actively with scientists in other parts of the world, including the United States and the U.S.S.R. The new giant radio telescope to be built in Australia will be the largest and most far-reaching piece of equipment of its kind in the world.

Some of the possibilities of this new field of knowledge of outer space, involving cosmic rays and the harnessing of these and other phenomena, might as yet be unsuspected, but it is essential that the serious decisions ahead of us in this field should be made by mankind and not just by individual nations. Outer space should be recognized as a field of international concern before it is too late; it cannot be regarded like the high seas, in which outside territorial waters anyone can do what he likes, and which have been the arena of competition for naval supremacy. The world's scientists have met the challenge of outer space, and Mr. Casey urged that it is for the political leaders to meet the challenge it presents in their own field of competence.

While outer space, nuclear energy and electronics are probably the fields in which current scientific and technical advances are the most spectacular and impressive to the ordinary individual, they are, he continued, only part of a much wider revolution in man's position in the universe resulting from research and invention during the past fifty years in practically every field of science and technology. Those fifty years have witnessed developments in the sciences as well as in medicine, agriculture and engineering much greater than in the preceding thousand years. This direct contact with such activities, both in Australia and in many countries of Asia under the Colombo Plan, has greatly impressed Mr. Casey with what has already been achieved by men of science and with the promise of the future. The tide of research and invention is flowing ever more strongly, and it is essential to consider the probable course of scientific development in the next fifty years. For the first time in human history, the whole world might have within its reach the attainment of high standards of material welfare and security.

In a passage reflecting H. A. L. Fisher's well-known reference in his "History of Europe" a generation ago to the abounding miracle of science, Mr. Casey added the qualification "provided we can live together in peace, and concentrate our energies upon the co-operative application of man's advancing knowledge to the control of our physical environment". On this ground he suggested that science must inevitably figure to an increasing extent in the activities of the United Nations and in the Specialized Agencies. There is, indeed, already a very considerable range of scientific activity to be found, for example, in the World Health Organization, the Food and Agriculture Organization, the Technical Assistance Administration, the United Nations Educational, Scientific and Cultural Organization, the International Atomic Energy Agency, the World Meteorological Organization and the Conference on the Peaceful Uses of Atomic Energy. Moreover, the International Geophysical Year is itself a striking and encouraging demonstration of the importance and practicability of international scientific co-operation in the attack on specific problems that call for the combination of several scientific disciplines or techniques.

Nevertheless, Mr. Casey believes that the United Nations could do still more to stimulate and encourage scientific progress and the application of its results, and could play a larger part in planning the strategy of scientific advance, particularly when advance is needed on many fronts and when the world's scientific resources are unevenly distributed. First, he suggested, in regard to research, that it would be useful for the United Nations to look at the total picture to find gaps, to look for promising openings, and to consider the adequacy of the men and facilities available for research that should be undertaken. Next, he suggested, the United Nations could consider the dissemination of scientific knowledge and the results of research, with a view of reducing the excessive lag between scientific discovery and its widespread dissemination and application. Thirdly, he referred to the place of science in education and to the need to recast our ideas as to the proper content of a liberal and humane education.

In this context, Mr. Casey pointed out that the problem of education is much wider than the production of qualified scientists to meet the shortage in particular directions in so many countries. Nor is it enough for educational authorities to add a

further subject to the curriculum, to push in a science subject and to take out one of the humanities. He believes that no one is educated who does not know something about science or who knows nothing but science.

Mr. Casey recognizes that all these questions in varying and sometimes overlapping ways fall within the sphere of the United Nations and some of the Specialized Agencies, but he believes that a more concerted approach is needed and that the appropriate body for this is the Economic and Social Council. In view of the relatively little attention given in the past to the idea of a concerted approach to the field of natural science, Australia considers that the Economic and Social Council should give it priority for 1959.

Finally, Mr. Casey suggested that the General Assembly should request the Economic and Social Council to examine the role of the United Nations and the Specialized Agencies in relation to the advance of science and to consider methods of stimulating research in most-needed directions. It should also examine methods of achieving a wider application, dissemination and understanding of new discoveries, taking account of the great inequalities that exist in the scientific resources of different countries.

Apart altogether from the merits of Mr. Casey's particular proposals, his address indicates keen interest in and real understanding of science by the Australian Minister for External Affairs. Moreover, his speech follows a remarkable address on modern science and civilization which the Australian Prime Minister, the Right Hon. R. G. Menzies, delivered to the Australian Medical Congress last March. The trend of thought in both addresses is strikingly similar, particularly in relation to the significance of the Earth satellites, their plea for devotion of the immense resources of science to the service of peaceful human needs and their recognition of the critical importance of a balanced education in which science and the humanities both find a place. Whether or not this is coincidence, it at least suggests that some of Australia's leading political representatives are likely to bring to the consideration of any issues in which scientific or technological considerations are involved genuine awareness of these considerations and a capacity for a balanced judgment.

Mr. Casey did not refer specifically to the discussions of a decade ago on the question of establishing United Nations Research Laboratories, but his recognition that little research could or should be done by the United Nations itself or in the Specialized Agencies, and that the great private and national research foundations and the universities should not be set aside or their work duplicated, suggests that he is fully aware of the practical difficulties and of the criticism those proposals received. Strangely enough, although in the meantime it has become even more apparent in certain fields of research that only co-operative effort will suffice to install and operate economically the expensive equipment necessary, this was not noted by Mr. Casey. The corollary, that no one country can hope to carry out at once all the scientific and technological research that is desirable, quite apart from other essential scientific activities, is the strongest argument for Mr. Casey's thesis, and, whatever its ultimate fate, it should at least contribute to an awareness notably lacking in Great Britain, in the Government and without.

As regards research, Mr. Casey did not advance any fresh arguments. It is, or should be, the function of existing bodies, such as, for example, the Advisory Council for Scientific Policy in Great Britain, to be looking continually for gaps in the front of research, for promising openings, and to assess the adequacy of man-power and facilities available. It is hard to see how it would be any easier on the international plane to find and bring together the men competent for this difficult task. Nor can effect be given to these recommendations without substantial change in the whole political climate and without political representatives of the calibre and outlook of Mr. Casey and Mr. Menzies. Moreover, it is probably still true, as Sir Edward Appleton has pointed out, that the unions organized under the International Council of Scientific Unions are the most useful instruments of international co-operation in science.

A more promising field appears to be in the dissemination of scientific knowledge, for here it is the political factors that have largely been responsible for the major obstacles. They could be removed by fuller understanding, as the success of the Conferences on the Peaceful Uses of Atomic Energy has indicated, but to reduce the time-lag between a scientific discovery and its widespread application can depend on economic and educational factors at least as much as on those that are directly political. There is, undoubtedly, a growing body of experience here that could be pooled, and it might well be that exploration of this proposal of Mr. Casey's could benefit Great Britain directly by bringing home to the Government the importance of certain factors in the dissemination of scientific information and the efficient use of trained man-power which it has been apt to neglect or disregard.

As Mr. Casey himself recognizes, this question is closely related to his third proposal regarding education. On this factor, more than anything else, depends the effectiveness of much of the work already undertaken under the Colombo Plan or through the Technical Assistance Administration to assist in scientific and technical developments throughout the world. If we can solve the problem of education on the lines he indicates, we shall have gone far to ensure the more efficient use of our existing resources in science and technology, quite apart from making it easier to expand that effort. Moreover, it is on the basis of such an educational policy that we can best hope to see the international co-operation that is undoubtedly required in the attack on some of the problems with which the widening horizons of science confront us, and the sustained support that the successful execution of an agreed programme demands. It should not be forgotten that it is one thing for the appropriate programme or project to be agreed and another for the resources to be allocated for its initiation. Even on

a national scale, that is not very easy, and it is unlikely to be easier on the international plane. No less important, however, is the continuing support of the project until it is complete. The difficulty which international organizations have hitherto experienced in securing such support from year to year warrants little optimism that, without considerable raising of the standards of education, integrity and objectivity in political circles at all levels, we can hope for the co-operation and sustained support required for an attack on any major scientific or technological objective on the scale necessary in the modern world. Mr. Casey's proposals may, however, lead to a clearer understanding of what is possible if the individual nations are willing to pay the price; and they remind the scientist and technologist once more that he has responsibilities in this matter of education which are not simply professional but those of the citizen, too.

LIFE OF HENRY ARMSTRONG

Henry Edward Armstrong, 1848–1937

The Doyen of British Chemists and Pioneer of Technical Education. By Dr. J. Vargas Eyre. Pp. xix+325+15 plates. (London: Butterworths Scientific Publications, 1958.) 30*s*.

THIS biography of H. E. Armstrong by one of his former pupils, Dr. Vargas Eyre, details the life of a vivid personality spanning the remarkably eventful years from 1848 to 1937. He began the study of chemistry at the Royal College of Chemistry just before Hofmann left to return to Berlin. Edward Frankland succeeded to Hofmann's chair in 1865 when the idea of chemical valency was emerging and before Kekulé's benzene formula was generally known. But before Armstrong left the stage, valency had received an explanation in terms of the electron, and the three-dimensional structures of such complex compounds as the sterols had been elucidated. Truly a remarkable advance in a single life-time, and the recent synthesis of the diamond in a tetrahedral anvil at pressures of 100,000 atmospheres and temperatures near 2,000° C. shows that the forward march continues.

In 1865 public sewers were almost unknown, and water pollution rampant. Frankland was one of those charged to tackle the problem and he set 'H. E.' to devise a method for estimating the pollution. During this period he attended lectures on geology by Ramsay, on physics by Tyndall and those on the place of science in education by Huxley. Later, Frankland urged him to go to Leipzig to work with Kolbe, and he did so in 1867 and remained nearly two and a half years working for his doctorate. On his first day in Leipzig, Kolbe suggested that Armstrong should examine the mixture formed on sulphonating phenol. Kolbe was also a forceful exponent of both attack and defence on chemical questions, and all the guiding principles in Armstrong's subsequent career had thus been fixed before he was twenty years old: purity of food and especially of milk and beer with the great problems of agriculture and health (Frankland), an abiding interest in geology (Ramsay), the life-long crusade on the teaching of science and its importance to industry (Huxley), the dominating role of sulphonation in his research work and the whole crowned by a dynamic character and a powerful debater (Kolbe). Apparently such characters no longer emerge from the mould in this plastic age.

On returning from Germany 'H. E.' started his teaching career at St. Bartholomew's Hospital and continued in this part-time post for twelve years. It is said he never received more than £50 a year for the work. Already in 1875 he was junior secretary of the Chemical Society, and when the senior W. H. Perkin retired he activated and came to dominate the Society after 1880. He was one of the first four professors appointed to the new City and Guilds Central College in 1884, and his research output began to mount. Many papers appeared on the sulphonation of naphthalene, others were on the terpenes, and particularly camphor. In 1888 he advanced the quinone theory to account for the colour of organic compounds, and both with pen and in debate he vigorously championed the role of water in electrolysis.

Possibly his many wide interests prevented him from making any great advances in the laboratory, but great credit is due to his school for producing chemists such as F. S. Kipping, A. Lapworth, T. M. Lowry, W. J. Pope, and W. P. Wynne among others. His forward vision embraced the importance of crystallography in chemistry and led him to appoint Henry Miers to lecture to his students on the subject.

The lack of suitable posts for chemists in industry at that time was reflected in the fact that he never had more than about a dozen senior students, and this probably influenced the authorities to close his chemistry department in 1911. After nearly thirty years of great service to the Central College he was given notice to quit without pension.

Armstrong was a fiery crusader who occupied the centre of the stage in many causes, but his advocacy of the teaching of science in schools also showed considerable statesmanship, as witness the paper he presented on the subject to the British Association in 1889 and its sequel in the successful trials of the heuristic method at St. Dunstan's College and Christ's Hospital. It is not too much to say that his work for education profoundly influenced science teaching in all English-speaking countries. It gives much food for thought that in spite of the urge for technical education and the application of science to industry in the fourth quarter of last century, these very problems are a matter of life and death to us in the third quarter of this century.

Dr. Eyre's account of Armstrong's life has clearly been a labour of love, and in the interest of the history of science it is well that it has been made. Perhaps it is rather long even for such an eventful life, and if much of the minor matter had been sacrificed Armstrong's great record of service to science and education would have shone all the clearer.

G. R. CLEMO

FRAUDULENT DOCUMENTS

Suspect Documents

Their Scientific Examination. By Dr. Wilson R. Harrison. Pp. viii+583. (London: Sweet and Maxwell, Ltd., 1958.) 84*s*. net.

THE book under review is a very important contribution to the published knowledge on the examination of suspect documents, particularly as it is the first complete review of the opinions of an acknowledged British expert on the subject.

Fraudulent documents have existed as long as genuine documents, and the problem of their detection has been of considerable importance to States and individuals. This problem existed before science was sufficiently advanced to assist in its solution and, therefore, there grew up a tradition of examination of documents based on superstitious credulity and with no scientific background whatsoever. It is against this tradition that the modern scientific document examiner has to fight constantly in courts of law and in public opinion. A. S. Osborn in the United States was the first to show successfully the necessity for the recognition of scientific principles in this sphere, and his "Questioned Documents", first published in 1910, is the classic on the subject. Other books of his, such as "The Mind of the Juror", indicate the difficulty experienced by the document examiner in divorcing the mind of the layman from preconceived ideas and directing it to the scientific facts which are demonstrably present in the examiner's report. In the 1920's and early 1930's, C. A. Mitchell in Great Britain most actively pursued and reported the search for scientific methods of examining documents, and a number of other authors have written on various aspects of document work; but little has been reported on the comparison of handwriting and typewriting, although considerable advances have been made. While Ordway Hilton in 1956 described American experience, the volume under review fills the gap from the British point of view, which has been created for a modern evaluation of existing techniques, and the book must therefore be read by all who are interested in these matters.

The book may be divided into four parts. First, the scientific examination of documents for alteration or fraud. This includes modern techniques such as, for example, the chromatography of inks. Secondly, the photographic techniques used in documentary analysis for various purposes are discussed, with the difficulties arising in making photographs for record purposes, and also the manifold special techniques required to detect alteration, erasure, obliteration, indentation, mutilation and all the other ways of ill-treating documents. Thirdly, handwriting and typewriting comparisons; these are extremely fully and authoritatively dealt with. Fourthly, the many requirements for obtaining the maximum use in court of handwriting and typewriting evidence are given, commencing with advice to the police in securing the best available material and ending with advice to counsel on the special problems arising in the presentation of handwriting evidence.

Each section is exhaustively and comprehensively treated and contains a mine of information for those wishing to understand the principles and methods involved.

There is some repetition, admitted frankly by the author, much of which is necessary both to ensure the completeness of each individual section and also to emphasize salient points. Nevertheless, I found that the repetition in Chapters 8–15 on handwriting and typewriting comparison, which the author undoubtedly has nearest to his heart, detracts from the enjoyment in reading the chapters.

The book is beautifully and carefully produced, and the illustrations are clear and informative. Only four minor proof-reading errors were detected, which is very few considering the size of the book. The index is comprehensive, and a glossary is included; this appears to be neither necessary nor helpful to the public for which the book is written.

L. C. Nickolls

THE LAND OF AUSTRALIA

Land Utilization in Australia

By Wadham and Wood. Third edition by Sir Samuel Wadham, R. Kent Wilson and Joyce Wood. Pp. xxii + 344 + 77 plates. (Melbourne: Melbourne University Press; London: Cambridge University Press, 1957). 40*s*. net.

THE first edition of this book, by Prof. Wadham and the late Gordon L. Wood, then lecturer in economic geography in the University of Melbourne, was completed in 1938 and published in 1939. The second edition, completed in December 1947, appeared in 1950, so that the three editions mark approximately ten-year intervals. In the meantime, the book has become an indispensable standard work. The story is now brought up to date partly with the help of Kent Wilson, who is lecturer in economic geography in the University of Melbourne. The senior author has become emeritus professor, and been knighted; Gordon Wood's daughter contributes a valuable new series of maps and diagrams.

These decades have witnessed some remarkable, sometimes curious, changes in land use in the continent. The early White settler had found the land of Australia more nearly virgin than any territory on Earth, for the aborigines, never numerous, neither tilled the soil nor kept herds of animals. They lived frugally by hunting and gathering edible fruits and roots with a minimum effect on the flora and fauna. If their presence resulted in occasional bush fires it is likely that at least as many fires were caused by lightning or other natural causes. At the same time the isolation of the continent had led to a balance between a peculiar flora and a peculiar fauna different from that anywhere else in the world. The physical environment of relief, climate and soil is repeated elsewhere, but the biotic environment is unique. It presented, and continues to present, difficult and challenging conditions to the spread of Western methods of both arable and pastoral farming. The decades preceding the uniting of the States as the Commonwealth of Australia in 1901 were characterized by a vast extension of cultivated acreage and of flocks and herds, and by a spirit of ebullient optimism. This optimism was part of the process of nation-building exemplified by the publication of such works as "Australia Unlimited". Lone voices, such as that of Prof. Griffith Taylor, in the nineteen-twenties, which dared to suggest there existed a dead heart of desert which could not be revived, were howled down. To-day the difficulties are realized: the strength and importance of physical factors, above all availability of water, are fully recognized.

The authors survey the historical sequence of settlement—wool, then wheat, then dairying, then irrigation agriculture, with each in turn coming to occupy a definite but by no means fixed position in the whole. The present position is that the total of cropland, including sown pastures and orchards, is only 2·5 per cent of Australia's 3,000,000 square miles. Although 55·8 per cent is claimed as natural pasture and rough grazing, much has a very low carrying capacity. The depression of the 'thirties had reduced the initiative and morale of the countryside, the varying phases of war demanded adaptations of farming which were quite impossible. At first Britain wanted all the wool, but no shipping was available for fruit and wine and little for wheat.

Then Britain, as Danish and other supplies were cut off, demanded vast quantities of dairy produce and bacon. The arrival of a million Americans resulted in an insatiable demand for orange juice and milk. The post-war period has seen its violent changes too—the 1951 inflationary demand for wool, and then the collapse of prices in 1952. Despite the vast reserves of land the present trend is rural depopulation, and the stupendous growth of Australian cities. Mechanization, with consequent reduction of labour force, and intensive development of the more favoured lands are characteristic of the present: the future may hold many surprises. L. DUDLEY STAMP

THE PAREXIC ANALYST

Applied Analysis

By Prof. Cornelius Lanczos. (Prentice-Hall Mathematics Series.) Pp. xx+539. (London: Sir Isaac Pitman and Sons, Ltd., 1957.) 55*s*. net.

APPLIED analysis—Prof. C. Lanczos suggests the adjective 'parexic'—is described by him as "the analysis and design of finite processes which approximate the solution of an analytical problem". The 'pure' analyst is, say, concerned with the existence of approximations to arbitrary functions by special types of functions, such as polynomials, to within an arbitrary ε, the 'numerical' analyst wishes to calculate the polynomial in some specific case, for an assigned numerical ε: the 'parexic' analyst is more interested in construction, and economy of construction, minimization and estimation of error, than in existence or calculation. Such a classification can scarcely be clear-cut; and the problems of the parexic analyst must in any event be modified by the invention of new computing devices, but a label for those interested as much in the theory as in the processes of numerical analysis may be useful. In some respects, the aims of the book resemble those of Householder's "Principles of Numerical Analysis", but Prof. Lanczos deploys on a broader front, in less detail and in a more discursive style. A sound knowledge of calculus and some acquaintance with the complex variable and Cauchy's theorem will will enable the student to read the book with ease.

The chapter subjects give a good indication of the main content, though not of the richness of the material: algebraic equations; matrices and eigenvalues; large-scale linear systems; harmonic analysis; data analysis; quadrature methods; power expansions. From a book full of interest, a selection of special items, even if depending on personal preference, may be worth making. Bernoulli's method is prominent in the chapter on algebraic equations, and complex roots, so important in stability criteria, receive much attention. The geometrical interpretation of matrices and eigenvalues, to illustrate their algebraic treatment, should greatly help the novice. The 'spectroscopic' method, which eases the calculation of small eigenvalues, is particularly dear to the author, since it allows him to exploit his favourites among the orthogonal polynomials, those of Chebyshev; indeed, these keep turning up aptly throughout the book in quite surprising places. The study of the inversion of the Laplace transform is most valuable, in the light of recent technical requirements, and Chebyshev plays a part. Numerical integration is centred on Gaussian methods, with a modification designed to avoid the troublesome evaluations at irrational points without serious loss of accuracy; the author ignores Chebyshev in this connexion, though his rules are, I believe, still much employed by naval architects. In expansion problems, the construction of expansions which shall furnish reasonably good approximations over a whole range, rather than very good at one end and poor at the other, is helped by using orthogonal polynomials, and here, as also in the related problem of speeding up convergence, the Chebyshev polynomials are again prominent, Finally, introductory historical paragraphs to each chapter help in setting the scene and preparing the reader for what is to follow. T. A. A. BROADBENT

CHROMOSOMES

Looking at Chromosomes

By John McLeish and Brian Snoad. Pp. vii+88 (48 plates). (London: Macmillan and Co., Ltd.; New York: St. Martin's Press, Inc., 1958.) 16*s*. net.

THE quality of a book of photographs must rest not on the technical standard of the photographs, for this is taken for granted, but on the suitability of the subject and on the discrimination and skill of arrangement. Chromosomes are certainly photogenic, but can their cyclical changes in shapes and movement be captured in a series of post-mortem stills? In trying to find an answer it is difficult not to make the unfair comparison with the enthralling films of live chromosomes that show every movement, relevant and irrelevant, in a most dramatic way.

The photographs in "Looking at Chromosomes" are so well chosen and arranged that they show the changes in shape and most of the relevant movements of the chromosomes. They cannot show the movement of chromosome arms or the unorderly jostling of the paired chromosomes for their place on the metaphase plate of meiosis which have been revealed in moving films. But the essentials for interpreting chromosome form and movement and their significance in heredity are clearly shown. The unique feature about the series is that the cyclical changes in mitosis in roots, in meiosis in the male pollen mother cells and female mother cells are all taken from one organism—the regal lily. This is no mean achievement, for most organisms have an obscure part of the chromosome cycle which is technically difficult to show. The short text of explanation emphasizes the genetic implication of the chromosomes. Two minor criticisms may be made here. The cytoplasm is described as "a highly viscous fluid". This is only true sometimes; often the cytoplasm is little thicker than water. The constancy of the complement of chromosomes is not so universal in differentiated cells as the over-simplified statement in the last chapter implies.

The addition of a simple time-scale of the chromosome cycles would add greatly to the completeness of the general picture.

For those who do not have a moving film of chromosomes or a projector, "Looking at Chromosomes" is quite the best and only complete account in photographs of our heritage—the chromosomes.

D. LEWIS

ELECTRON MICROSCOPY IN BIOLOGY

By Prof. R. D. PRESTON, F.R.S.
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INVESTIGATION of biological structures smaller in dimension than the resolution of the light microscope has until comparatively recently been confined to a relatively few laboratories throughout the world. This was because the physical principles involved were such as to be unfamiliar to the majority of biologists and because the equipment required was normally not found in their laboratories. Apart from the replacement of visible light by ultra-violet light in the conventional type of light microscope (increasing the resolving power by a factor of about 2) the methods used were those of polarization microscopy and X-ray diffraction analysis. With neither of these two methods was it possible to produce directly a visual image of the structures being investigated; a complex mental process intervened between the observations made and the structure delineated. The methods suffered, moreover, from other serious drawbacks. Only structures which were crystalline could be investigated, that is to say, substances with atoms and molecules arranged in a regularly repeated order in space. The smallest objects which could be studied were microscopic in size, and the observations made upon them frequently enabled only an 'average' structure over the whole specimen thickness to be determined. Again, whereas in the light microscope the smallest dimension directly observable is of the order of 1000 A., the power of X-ray diffraction analysis lies in the dimension-range of a few angstroms, and even the method of low-angle scattering enables the form of an object to be calculated only up to a dimension of a few hundreds of angstrom units. This left a wide gap of structure completely outside the scope of investigation.

In electron microscopy, biologists have been presented with a tool which, while not free of its own drawbacks, and not in any sense replacing the older methods, has removed some of the particular disadvantages inherent in these methods. Moreover, the preparative techniques and the observational methods are basically those of light microscopy, in which biologists already excel. This newer technique has therefore thrown the field of submicroscopic structure open to biologists, and the opportunity thus given has been taken up vigorously by biological departments throughout the world. This constitutes a revolution in histology perhaps of equal rank to that heralded by the development of the compound light microscope during the past century. The meeting held recently by the Linnean Society on applications of electron microscopy to biology, the first meeting in Britain confined solely to biological applications, demonstrates clearly the rapid progress which has already been made in this field, so rich in promise.

The use of this comparatively new instrument is not without its dangers, and these fall especially heavily upon the biologists. The specimen to be observed must be sufficiently thin to be penetrated by the electron beam. At best, therefore, the specimen thickness can be no more than 0·1μ and preferably, for high resolution, not more than 100–200 A. It is observed in a high vacuum, and is therefore completely desiccated, and the absorption of electrons causes a considerable rise in temperature. With biological material particularly, therefore, the investigator must at every stage, both in preparing the specimen and during observation, be prepared for the development of artefacts. At all stages and with all specimens it is highly desirable that results of electron microscopy should, in the first instance, be checked against observations with the older and more familiar techniques.

Observations in the electron microscope can be interpreted with the least ambiguity with specimens of robust material the structure of which is already fairly well known. Such a material is the plant cell wall. Some cell walls lend themselves to preparation for observation by relatively mild mechanical treatment, and the wall of *Valonia* vesicles is particularly convenient. This was historically the first organism yielding an electron micrograph of relatively untreated cell wall material[1]. There rapidly followed a succession of publications[2] on other wall material usually prepared by grinding in a blender. It soon became clear that the first observation, that the cellulose consists of long narrow threads (in *Valonia* of the order of 200 A. in diameter), is of universal application in the plant kingdom (Fig. 1). This harmonized completely with the already known structure of cellulose in the form of long molecular chains of β1–4 linked glucose residues lying, sometimes more, sometimes less, parallel to each other. With *Valonia*, in particular, these long threads—termed 'microfibrils'—were found to be arranged parallel to each other with sufficient accuracy and to be sufficiently crystalline to give an electron diffraction diagram in the electron microscope (Fig. 2). This diagram fully confirmed that the microfibrils consist in the main of long molecular chains of glucose residues lying parallel to each other and in large part spaced in a regular crystalline space-lattice. This combination of electron microscopy with electron diffraction analysis of identically the same specimen observed in the electron microscope offers the biologist a most powerful tool in the study of material to which these methods can be applied. Not only can a visual image be recorded but the molecular structure of the material can also be determined, a combination which has already led to some most spectacular results[3], including the demonstration of the clear necessity for a re-determination of the unit cell of cellulose derived by the method of X-ray analysis.

The more recent use of ultra-thin sectioning and of surface replication[4] has served largely to confirm structures already revealed for a wide variety of cell walls by the older methods of polarization microscopy and X-ray diffraction analysis[5]. Moreover, the visual delineation of structure in minute pieces of material which electron microscopy allows has enabled considerable advances to be made in the question of the synthesis of cell wall materials. Thus, it has been

Fig. 1. Electron micrograph of a single lamella of the wall of the vesicle of *Valonia ventricosa*, palladium-gold shadowed (× 40,000) Note the parallel microfibrils occasionally twisted
Fig. 2 (inset). Electron diffraction pattern of a lamella similar to that shown in Fig. 1, but unshadowed, and in correct orientation with respect to Fig. 1. Note the line of arcs along the equator (parallel to the shorter edge of the page) perpendicular to the length of the microfibrils in Fig. 1

reported[6] that, whenever a wall lamella is observed which is just being laid down by the cytoplasm, the wall surface is covered by a series of aggregations of corpuscular bodies from which cellulose microfibrils appear to diverge. The observation of the first formed wall around swarmers has already produced results of outstanding importance from this point of view[7], and present and future work on this material is of the greatest promise. Again, once more in harmony with the older work, it has turned out that the microfibrils in the walls of growing cells are arranged more or less transversely to cell-length, particularly in the innermost wall lamellæ abutting upon the cytoplasm. It is claimed that the outermost layers of such cells, away from the cytoplasm, are constituted of microfibrils which are more nearly randomly or even axially oriented. On the grounds of these electron microscopical observations, Roelofsen[8] has proposed a hypothesis to explain the relationship between the expansion in area of the cell walls of growing cells with the growth of the cell. On this hypothesis, in a freely growing cell, the microfibrils are first laid down by the cytoplasm more or less transversely to cell-length and, as the cell elongates, this lamella, moving outwards through the wall as newer lamellæ are laid inside it, becomes elongated through the agency of turgor forces so that the microfibrils become progressively oriented more and more away from the transverse. While such a mechanical explanation of the reaction of the wall to growth processes has not met with universal acceptance, and while the hypothesis makes no attempt either to explain how the microfibrils come to be arranged transversely or how it is that cells elongate rather than increase uniformly in dimensions, it does include principles which cannot be ignored in discussions of the growth process.

Considerable attention has been paid to the construction of plasmodesmata in primary walls and pits in secondary walls[9]. It has become clear that plasmodesmata are indeed penetrations of the wall by cytoplasm which runs among rather loosely packed microfibrils, and that the membrane of bordered pits consists of a loosely woven network carrying the central torus when a torus occurs. Along more or less the same lines, it has similarly been shown by observation of ultra-thin sections that the pores in sieve plates of *Cucurbita*[10] and of other species[11] are completely filled with cytoplasm, a simple observation which seems to rule out all existing theories of phloem transport except those involving the use of metabolic energy.

Among those whole organisms which can readily and simply be observed in the electron microscope, the viruses and the bacteria are, of course, outstanding. The beautiful electron micrographs of Wyckoff and others have shown how readily the shape and size of virus particles can be demonstrated[12] as well as the beautifully regular way in which these particles become associated to form crystals[13]. The bacteria have been examined both whole and in ultra-thin section[14] so that these minute organisms are now open to critical examination.

It is, however, perhaps in the cytoplasmic organization both of plants and of animals that electron microscopy, and especially the observation of ultra-thin sections, reaches greatest power. Here structures are being revealed which were not known before the development of electron microscopy, and it is therefore in this field that artefacts have most carefully to be excluded. It is impossible in this short space to mention even briefly all the important observations which have already been made in this field, and the choice of illustrative material here is therefore quite arbitrary. Considerable attention has been paid to those elongated organs known as flagella which by movements of various kind propel motile cells through the substrate. Whereas with motile bacteria[15] the flagella appear to be simple fibrils, all flagella so far investigated in higher plants and animals[16] appear to be multiple and to contain eleven separable strands (Fig. 3). Ultra-thin transverse sections of these flagella have shown that these eleven strands are arranged in a specific manner, two central strands being surrounded by nine others arranged more or less in a cylinder. In the spermatozoids and other motile cells of some plants the flagella are clothed with a mat of fine fibrils—to which the German name 'flimmer' is applied—and occasionally with spines and hooks in an intriguing array. These observations are even at present of considerable taxonomic importance and may well pave the way for an understanding of motility in these motile cells. Current research is aimed at tracing the connexion between the bases of these fibrils and the internal organelles of the parent cells.

The cytoplasm itself has provided a wealth of structural detail (Fig. 4) and the larger granular inclusions have naturally been the first to demand attention. Within chloroplasts, for example, it has been confirmed that the chlorophyll lies in the so-called 'grana' and that both the grana and the ground substance are laminated. High-resolution microscopy has further demonstrated that these

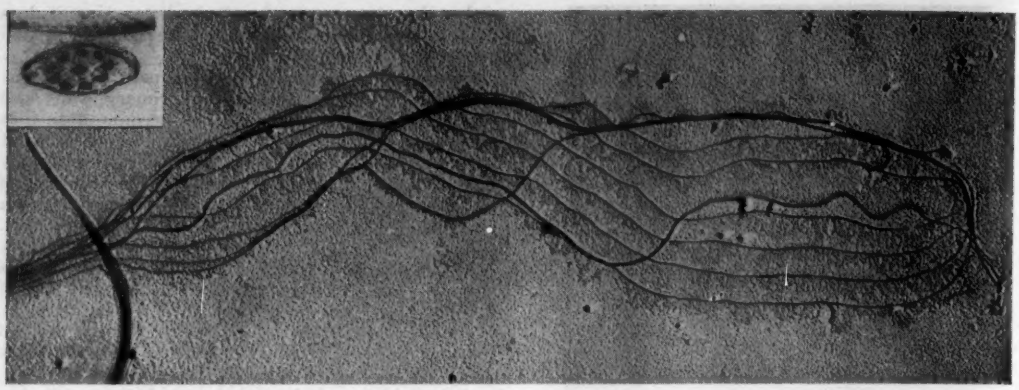

Fig. 3. Electron micrograph of an intact and dismembered flagellum of a *Sphagnum* spermatozoid (× 5,500). (Manton and Clarke, 1952) Inset: Electron micrograph of a transverse section of a flagellum of a *Sphagnum* spermatozoid (× 38,000). (Manton, 1957.) (Photographs prepared by B. Clarke)

lamellæ are often double and folded in complex ways[17]. This again confirms the opinion often expressed, based upon the physiological observations of the absorption spectra and fluorescence spectra of chlorophyll in solution in the leaf and as a sol. Mitochondria have similarly been shown to possess a membrane from which peg-like protrusions stand out towards the inside of the granule[18]. These protrusions have been shown in several instances to be double and may be infoldings of a membrane. The question of the presence of a membrane around the nucleus in the resting phase has been answered once and for all. Both in plants and animals the nucleus has a clearly marked membrane which is double and which is perforated at frequent intervals[19]. Little definitive evidence has yet been presented in electron micrographs concerning the structure of chromosomes.

The structure of the cytoplasm surrounding the more obvious granular inclusions has proved to be more complex than speculations, based on observations under the light microscope and the physical properties of the material, had led us to expect. It is undoubtedly in this field that the greatest care has to be taken in preparing the specimen in order to prevent the development of artefacts. The general appearance of the more organized cytoplasts is that of a series of vacuoles limited by fine membranes of the order of 100 A. or less in thickness which are probably double. This reticulated appearance gives the impression that the cavities lying between the membranes are empty. It must, however, be realized that the complicated imbedding technique, including the imbibition of methacrylate monomers, may cause solution of cytoplasmic constituents and therefore their disappearance from sections. It should be realized, too, that the pH of the fixing fluid is highly critical and that the only criterion at the moment for the suitability of any particular fixation method lies in the clarity of the resulting electron micrograph. More complicated regions such as the Golgi apparatus[20] have clearly been identified and the structure worked out. The widespread appearance has been noted of a well-marked reticulate system consisting either of vesicles or long narrow canals or tubes or plates bounded by double membranes, named by Porter and Kallman the 'endoplasmic reticulum'[21], provisionally interpreted as being associated with conduction or circulation of various substances.

Electron microscopy has thus made it clear that one common theme seems to run through the structure of the whole of the cytoplasm and its inclusions, namely, that the structure is based on a lamellated system, and it seems that biochemical activity is specifically associated with lamellæ. This is, of course, entirely in harmony with the generally accepted view, based on physiological evidence, that metabolic processes occurring in cells are associated at some stage with an adsorption phenomenon at surfaces.

In addition to this direct attack on biological problems by the method of electron microscopy, it must not be forgotten that the electron microscope is playing a great part in an indirect way, too, in the

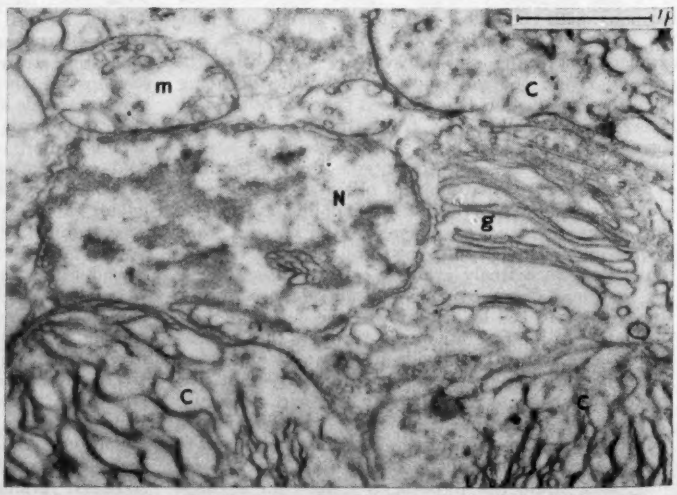

Fig. 4. Section of a cell of *Chrysochromulina chiton* (a marine flagellate) showing nucleus (*N*), parts of three chromatophores (*C*), mitrochondrion (*m*), a Golgi area (*g*), etc. Unshadowed (× 22,500). (Parke, Manton and Clarke, 1958. Photograph prepared by B. Clarke)

development of the biological sciences. Thus, the localization of ribonucleic acid or of enzymes and enzyme systems on cytoplasmic particles of submicroscopic dimensions[22] could not have been achieved without the simultaneous electron microscopical observation of the particles and the verification that the material under investigation contained no other bodies. Again, in the chemical fractionation of biological material the results are on a much surer foundation now that it is possible to check the purity of the extracts by electron microscopy. One case in point refers to the extraction of plant cell wall material[23] in which the extraction was watched under the electron microscope at each stage, so that not only could the chemical composition of the material be given but also the site from which the various components had come could be located with some precision.

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CONSERVATION OF NATURAL RESOURCES

THE International Union for the Conservation of Nature and Natural Resources held its sixth General Assembly (and seventh Technical Meeting) in Athens during September 10–19, under the presidency of Prof. R. Heim of Paris. The main theme of the technical discussions was that of soil and water conservation, one so wide that it was necessary to subdivide the papers submitted (by delegates from more than thirty countries) into groups dealing with the technical aspects of evaporation and run-off, the use of vegetation in the control of erosion, the effects of dams on habitat and landscape, and the development of aquatic resources, as well as the ecological solutions of specific water and soil conservation problems. In a special address to the assembly, Dr. R. Scott Russell gave a thoughtful and interesting analysis of the problems set by the influence of atomic radiations and wastes on the vegetation cover.

The rapid development of ideas of water control was well illustrated by attempts to see in evaporation from land surfaces with different types of vegetation cover, variants in the eddy-diffusion systems which might exert comparatively little influence on the over-all evaporation-rates of a considerable tract of country. Much attention was directed to the influence of the vegetation or other cover on the soil temperature and indeed to the energy relations of the evaporating surfaces, and the physical conditions which determined how rapidly water ran off or sank

out of reach in the soil. H. C. Perriera, in particular, showed the importance of studying 'rainfall acceptance' and the conditions governing the structure of soils in this connexion. W. Robyns thought that in tropical regions the role of a permanent vegetation cover in maintaining the hydrological equilibrium was of the first importance because of its influence on the temperatures and structures of soils, and on biologically induced fertility. Thus, although several lysimeter studies from various parts of the world were reported, the results from them were generally regarded as open to various interpretations, giving little final assistance in solving the physical problems of semi-arid soils.

Considerable attention was also devoted to the use of dams to impound water for irrigation or for general industry. The losses of water occasioned by different sizes of dam and diverse types of dam distribution were compared with those from other forms of utilization, with some tendency to conclude that water was best used where it fell, particularly in regions requiring protection from desiccation or soil erosion. The value of fish culture in impounded waters as a source of protein food was regarded by some speakers as a compensation for any water losses.

It was made extremely clear that conservation of water is of the first importance in most countries, particularly in the highly industrialized and the arid, and that the problems involved in wise planning and utilization are rarely those for the engineer alone but are likely to involve not only the physicist and pedologist but also the meteorologist, plant physiologist and ecologist, often in conjunction with forester and agriculturist.

Much attention was naturally directed to problems in the Middle East, North Africa and the Mediterranean region generally. Several speakers adopted a historical approach to conservation of water and erosion of soil, very appropriate against the background of ancient Greece. They saw in deforestation and in wasteful and ignorant methods of land use the reasons for the decline of Mediterranean civilizations, the lessening of cultivable land and the spread of semi-desert conditions in this region. The arguments developed and evidence produced were in marked contrast to the well-known views of Huntingdon and others which base changes of this type on a supposition of climatic desiccation. G. V. Jacks threw still another idea into the arena, the conception that a society's socio-economic status determines whether it is 'fertility-destroying' or 'fertility-creating'. "Thus the capacity of the world for food production is limited not by land or soil-fertility but by the productive capacity of its urban industries," which will be balanced by an equivalent energy in agricultural development. "A wealthy city will create a productive soil," and the relative scarcity of large cities in the Mediterranean might thus imply low productivity.

The technical papers almost always led to general discussions involving the world background of rapidly increasing populations and the over-riding problem of how to marry the need for increased production with the preservation of natural resources, either as a long-term economic need or for scientific or amenity aims. As this assembly showed, the Union is becoming a meeting-ground between those whose aims lie chiefly in production and those who are mainly interested in the protection of Nature and natural resources. Edward Graham remarked that those who emphasize the need for protection or for production are respectively contrasting, on one hand, the necessity for the maintenance of the stability of natural environments and their organic life and, on the other hand, the manipulation of habitats in order to obtain the organic products required. It is becoming evident that these rival aims are nearer than is often thought, for the 'marginal' or more extreme habitats need protection if they are to be at all productive, and, in contrast, high production can only be based on those habitats which are able to withstand manipulation, that is, are ecologically so 'buffered' as to permit a considerable latitude in treatment. Conservation, therefore, consists essentially in the identification and classification of environments followed by the development of protective and stabilizing forms of production for ecological systems which are unstable. A paper by forestry representatives of the Food and Agriculture Organization was of interest in this connexion, because it described how, in scrubby protection forests in semi-arid regions, the use of branches and small timber for the production of charcoal in specially devised kilns had made it possible to maintain the necessary permanent vegetation cover and yet produce a necessary fuel for the inhabitants.

The multiplicity of considerations involved in conservation often makes it difficult to popularize the basic conceptions. While it is evidently the role of scientists, on one hand, and of government, on the other, to deal with multiplicity of factors and of aims and with their integration, conservation and the "real future of all natural resources (again to quote Edward Graham) lies in the hands of the peoples themselves, for it is they who till the fields, graze the flocks and cut the forests. If the people are to care for the land they must have a stake in it. For this reason, ownership of the land, or at least a share in the proceeds of its production, becomes important".

If the science and technology of the management of resources are to be brought within the people's reach, local organizations are required not only to unify the efforts of the local community but also to utilize, in full, the technical assistance which may be made available from government. Only by such means can the work done become part of the pattern of living and culture of the community. The role of education is equally important, and both these aspects of the problem were considered to be particularly urgent in under-developed countries, where the uncontrolled growth of populations is likely to lead to over-exploitation and to the irreversible destruction of natural assets and amenities. Education in such societies will involve not merely the spread of technical information but also the need for the indigenous inhabitants to acquire a feeling of responsibility for the resources of their land and its wild life. This must be coupled with the presentation of necessary ideas on conservation both to industrialists who may seek to exploit present conditions at the expense of the future and to administrators who must acquire a long-term outlook with a capacity to supply leadership in balancing immediate demands for exploitation against the need for preserving the natural heritage for the future. In discussing the measures which might be adopted to bring about these threefold aspects of education, the assembly concluded.

W. H. Pearsall

ADVANCES IN THE USE OF RADIOISOTOPES

Medical Uses

THE developments which have occurred in the use of radioisotopes in medicine, as doubtless in other departments of science, have usually been associated with technical developments on other lines also. The availability of radioisotopes as a tool stimulates the imagination and ingenuity of those using it. This has been reflected in the past in counter techniques; but the development of chromatography, scintillation mapping, methods of section-cutting, autoradiography and other techniques are all reflected in the papers submitted to the second International Conference on the Peaceful Uses of Atomic Energy.

In biochemical work one of the most important developments has been the use of tritium, which, by virtue of its soft beta-radiation, permits the localization of uptake of a labelled compound, thymidine, within 1μ of the structure taking it up, so that accurate information is obtained on chromosome duplication and the timing of synthesis of deoxyribonucleic acid, nucleolar synthesis of deoxyribonucleic acid and cell migration from crypts to villi in the intestinal epithelium (*P*/842). The necessity for correction for the absorption in protoplasm and the effects of nuclear flattening was stressed in another paper (*P*/323), since these factors must influence the effect on the photographic emulsion. Only metabolic reactions can detach the tritium from the labelled thymidine, but tritium in high concentration may give large doses of radiation locally as well as having different metabolism from hydrogen.

Much of the Russian work on animals has focused attention on the central nervous system, and in this respect they have shown (*P*/219) that methionine-^{35}S is an essential amino-acid for the cells of the brain and is synthesized into protein. An interesting investigation of protein synthesis (*P*/846) demonstrated the relatively sudden synthesis in 6·5 min. of the ferritin molecule by using valine-^{14}C. It is emphasized that it occurs directly from amino-acids and not from polypeptides or larger molecules. A relatively comprehensive review of protein metabolism determined by radioisotope methods was given (*P*/77). The investigation of detailed metabolic processes was exemplified by the demonstration of the citric acid cycle in yeast using carbon-14 dioxide (*P*/1563), the relationship of phosphoryl choline, phosphoryl ethanoline and phosphoryl serine into phospholipids in the central nervous system (*P*/2318) and the use of phosphorus-32 and paper chromatography to show the stimulating effect of glucose on phosphorus-32 turnover in muscle, kidney, liver and intestinal mucosa (*P*/1006).

In connexion with the skeleton, phosphorus-32, calcium-45 and sulphur-35 have been used to follow the metabolic processes of healing fractures (*P*/1500). The rapidity of concentration of calcium-45 in bone (commencing in 45 sec.), together with the rapid burying of calcium-45 and strontium-90 in the inaccessible regions of bone crystal (*P*/2397) and the demonstration of high concentrations of these isotopes in young Haversian osteons, all throw fresh light on the dynamic nature of bone metabolism. The metabolism of ruminants (*P*/813), the synthesis of milk (*P*/812) using carbon-14 labelled compounds and the isolated udder (*P*/852) have been investigated in detail. In connexion with hæmatology, the relationship of vitamin B_{12} labelled with radiocobalt to the intrinsic factors of the pig's stomach has been studied (*P*/1050), while in rats, incorporation of iron-59 has been used to study the factors influencing the formation of erythropoietin and to fix the kidney as its site of production (*P*/847). Survey autoradiograms of sections of whole mice have shown the distribution of various labelled drugs throughout the body (*P*/164), while in goats and cattle the metabolism of tritium-labelled hexœstrol has been demonstrated (*P*/280).

Several communications were concerned with radioiodine studies, and of these the relationship of the depression of central nervous activity due to damage to the pituitary or hypothalamus to inhibition of the thyroid seems important (*P*/2202). This has been investigated by the use of the defensive conditioned reflex, which has no effect in the absence of both the hypophysis and the adrenal. It would seem desirable that the conditioned reflex should be developed and used in other countries besides the U.S.S.R. as a tool for studying cortical function. Using this technique, it is stated that 0·5 μc. sodium-24 was a threshold dose for a rat, while to shorten the defensive conditioned reflex time to its initial level in 8–10 days a dose of 50 μc. of sodium-24 was effective (*P*/2056). Even tracer doses of iodine-131 are said to have significant effects.

Diagnostic measures using radioisotopes have become very numerous and varied. Iodine-132, with a half-life of 2·3 hr., permits early repetition of tests and, for the same precision, gives smaller doses to gonads, bone marrow and thyroid (*P*/277). It also makes possible the day-to-day following of conditions of iodine metabolism in the patient. Its preparation from tellurium-133 (half-life 77 hr.) is quite practicable. Much work has been done to elucidate thyroid metabolism. The etiology of thyroid disease and the scintillation mapping of the uptake of iodine have been improved. Pulmonary ventilation and circulation can be investigated alongside a cyclotron which can produce oxygen-15 with a half-life of 2 min. Decay of oxygen-15 is by emission of a positron, and the annihilation gamma-radiation can be measured by a scintillation counter externally (*P*/278). Small regions of the lung can be investigated, so that the method is an advance on bronchospirometry. Analysis of cardiac action has been advanced also by intravenous injection of radioiodinated serum albumin and also large-particle radiogold colloid. This latter is held by the lung capillaries and so normally excludes the circulation of the left heart (*P*/1385). Inhalation of krypton-85 and methyliodide-^{131}I has been used with the object of delivering a radioisotope to the left heart, so as to study the pure left-heart circulation (*P*/215) by external counting. Liver function has been studied by counting over the liver after the administration

of rose-bengal labelled with iodine-131, since the liver cells take up the dye (*P*/870). The use of a new substance, di*iso*propylphosphofluoridate, for labelling blood cells has the advantage that it is not eluted from labelled cells and is chemically inert. The life of human erythrocytes, 110–130 days, was confirmed, and leucocytes and platelets, since they also contain esterases, also bind di*iso*propylphosphofluoridate (*P*/557). The use of iodine-131 and diiodofluorescin for improving accuracy of localization of brain tumours (*P*/2069) was reported in connexion with electroencephaloscopy. Automatic scintillography is becoming more widely used, and (*P*/1219) facilitates the mapping of organs containing gamma-radiators. The possibilities of quantitative estimation of elements subjected to neutron bombardment have been exploited in the case of arsenic determinations in hair, finger nails and tobacco (*P*/69).

Consideration of the radiation hazard has been the rule in almost all the techniques discussed. The physician and the investigator alike recognize their serious responsibilities for this aspect of work with radioisotopes. Methods of measurement have advanced so much that small trace quantities are the role, even for the scintillation scanning techniques. The measurement of bremsstrahlung from phosphorus-32 is a definite advance (*P*/1222) which may develop into a useful method.

In the therapeutic use of radioisotopes, no radically new procedures were reported. The selective uptake of boron compounds by brain tumours has been previously reported, and the work is being improved in detail. Boron-10 and lithium-7 have been concentrated to an effective degree in brain neoplasms, so that neutron capture can give a selective radiation effect on the tumours (*P*/881). The five-year results of the use of radiogold colloid intraperitoneally for ovarian cancer show a 45 per cent survival without symptoms from fifty-one patients. The results are the best yet published (*P*/234) for any series of ovarian carcinoma including all stages. Interstitial uses of radiocolloids of gold, yttrium and phosphorus have been explored by several workers. Uses of cobalt-60 for intracavitary treatments have been developed further (*P*/973). Attempts at destruction of the pituitary gland by grains of radiogold (*P*/68) and by radioyttrium pellets (*P*/874) are not by any means uniformly successful nor free from complications, although a stereotaxic method seems less liable to complications than fluoroscopic methods. Teletherapy units containing cobalt-60 have been developed so as to provide the advantages of high penetration, without excessive damage to skin and bone. There is no reason for expecting bone marrow to be spared by these high-energy beams. The differences in techniques necessary to use these advantages were discussed (*P*/67) and the relative merits of cæsium-137 as an alternative were mentioned (*P*/2403). At the same time, it was stated that 314 units containing in all 179,000 curies had been distributed by March 1958 to eighteen countries by Canada and the United States alone. Cæsium-137 for short-distance beam units was described (*P*/579).

Some results, for example, 45·4 per cent alive without symptoms for two to five years of cases of living cancer and 31 per cent of cases of cancer of the œsophagus alive without symptoms from one to three years (*P*/2056), are better than one finds in most countries.

F. Ellis

General Uses

The sessions on isotope applications at Geneva covered a very wide field. There were few revolutionary disclosures, perhaps because only a year has elapsed since the Unesco meeting on isotopes was held in Paris. Isotopes are now employed in some sixty different countries, and the papers accepted amounted to about fifty in each session, although only eight were read. The standard of the papers delivered was uneven, suggesting that their selection was made partly from political considerations and not solely on their scientific merit. The variety of topics covered makes classification under headings difficult, and in a brief report one can only suggest trends and pick out items here and there that caught the eye.

The monetary savings made by use of isotope applications run to large figures. Libby's estimate for 1957 savings in the United States is 500 million dollars (*P*/2390). A Russian survey gave their figure for 1957 as 1·5 billion roubles. The United Kingdom figures are still being analysed and are likely to be in the region of £1 million saved.

Of the materials produced, there have been improvements both in quantity and quality. A much greater range of labelled organic substances is offered. These are prepared by standard methods of synthesis, by biosynthesis using growing plants or algae to incorporate the labelled atoms, or by radiation labelling. This latter method attaches the labelled atom by an exchange reaction usually following ionization caused by gamma- or beta-bombardment (*P*/284). There is a significant increase in the use of tritium as a label. Iodine is still the medical tracer most used, its scope being widened by the short-lived isotopes now made (*P*/277). Many countries have plans to step-up their production of fission products from their power reactors. Cæsium-137 will be used for commercial radiations in million-curie quantities in a few years (*P*/831). The use of krypton-85 is expected to grow for applications in the oil industry and for exciting luminous signs and lamps (*P*/2520). Strontium-90 will also be on the same scale; but so far no one has suggested a satisfactory method of containment of this toxic substance without impairment of its beta-radiation. The demand for cobalt-60 is increasing steeply. There are 160 cobalt-60 therapy installations of 1,000 curies in the United States alone. Within a few years there will be several massive radiation cells in operation using 10^5 to 10^6 curies each.

In the field of massive radiation, greater caution was noticeable than in the predictions made at the first Geneva Conference (*P*/65). Preservation of foodstuffs has been found to have a number of drawbacks in practice. Some excellent Russian work has been done on the preservation of potatoes and the chemical effects of the radiation on the tubers (*P*/2131). Feeding trials in the U.S.S.R. have led the Ministry of Health there to permit irradiated potatoes to be sold and eaten by the public (*P*/2308). Other papers reported promising results from ante-mortem injection of adrenalin into meat to be irradiated by gamma-radiation (*P*/258). This arrests the enzyme activity and avoids unpleasant changes in flavour and smell.

Graft and block polymerization of plastics under gamma-bombardment may soon produce some important products (*P*/826). The United States papers

reported a styrene–polyethylene ion-exchange membrane that has been used for purifying brackish water (*P*/2390). The possibility of coating some of the synthetic fibres to reduce their static attraction is of considerable interest to the textile industry. Improvements are reported from catalysts which are subjected to gamma-bombardment (*P*/2380).

A wide variety of industrial applications were reported at Geneva. In oil-well logging, radioactive methods are used as a standard technique. In 1957, eight million metres of oil boreholes were logged with neutrons. The movement of silt in harbours and estuaries can be measured with great sensitivity by depositing radioactive substances (*P*/2357). New methods of attaching the activity to sands and stones are being evolved, among them a Portuguese system of immersing sand in a radioactive silver solution which is later reduced by sunlight on the sand grains (*P*/1820). Measurement of flow in rivers, sewers and pipelines seems capable of application even on the largest scale. The recent method of total counts developed by Hull is a powerful variation of the usual technique (*P*/817). For tracing water through different strata, labelling by tritium, iodine or by cobalt complexes may show advantage in preventing the absorption of activity in the particular soils (*P*/1613).

Radiometric analysis is suggested as a control against toxic gases in the atmosphere (*P*/2390). The gas is made to react stoichiometrically with a radioactive reagent, and the resulting active product may be used to detect the gas quantitatively.

Several countries reported using tracers for mixing and flow studies to follow wood chips in pulp mills, and bulk flow in cement kilns, glass-works, etc. (*P*/1101). In most cases the measurement need only be made once, but it can give the information on hold-up and throughput-time vital to such processes.

Once again the papers from the U.S.S.R. showed their wide applications to the metallurgical industry (*P*/2218). Papers ranged from tests on mixing and melting times in steel furnaces and ladles to the study of micro-structure of alloys using autoradiography (*P*/2236).

In chemistry and biochemistry, the variety of labelled compounds has led to better understanding of chemical reactions and especially in carbohydrate, fat and protein metabolism. Thymidine, a precursor of deoxyribonucleic acid, has been labelled with tritium, so permitting autoradiography with clear enough resolution to study single cells or chromosomes (*P*/323). Further work continues on the mechanism of photosynthesis using chromatography and autoradiography. One method for following the path of oxygen starts with enriched stable oxygen-18. Later on, a chromatogram is bombarded by protons with the reaction $^{18}O(pn)^{18}F$ to allow the radioactive fluorine-18 to be measured (*P*/2520). Alpha-cameras were described for measuring thin paper, tissue or other microtome sections (*P*/1621). The surface densities measured were 10^{-14} gm./cm.^{2} with the claim that this could be improved to 10^{-15} gm./cm.^{2}.

A novelty was a Japanese method of using autoradiography to develop fingerprints by using formaldehyde or stearic acid labelled with carbon-14 on the protein traces in the print (*P*/1342). As the autoradiographs may require a week to develop it seems of questionable value for the speedy apprehension of a criminal.

In agriculture, work continues on the uptake of plant nutrients and the behaviour of ions in different soils (*P*/287). Of particular interest is the question of foliar sprays versus conventional root feeding (*P*/2390). Systemic insecticides and their subsequent fate in the plant are traced in the same way. Several nations described improvements to crops by selection of mutated strains. Gustafsson gave details of Swedish Pallas barley developed since 1947, which is an erectoid type having stiff straw and gives yields a few per cent better than its parent Bonus (*P*/2468). A Russian paper gave details of improvements in mutated types of streptomycin, aureomycin and terramycin which would save considerable amounts of money (*P*/2436). Even at the time of writing, some papers are still not available, and one looks forward to the publication of the official proceedings so as to re-read in comfort many of the contributions.

W. S. Eastwood

PROGRESS OF THE RUSSIAN EARTH SATELLITE *SPUTNIK* 3 (1958 δ)

By D. G. KING-HELE

Royal Aircraft Establishment, Farnborough

THE third Russian Earth satellite was launched on May 15, 1958, into an orbit which, like that of its predecessors, was inclined to the equator at an angle near 65°. On entering its orbit the satellite split into five pieces. The most important piece, carrying the instruments and radio transmitter, was roughly conical in shape, 12·3 ft. long and 5·7 ft. in diameter; it weighed 2,926 lb., including 2,134 lb. of scientific equipment, and was designated 1958 δ 2. The second and largest piece, 1958 δ 1, was the empty shell of the rocket which had carried the satellite into orbit; its shape and size have not been revealed. The other pieces, which have been observed only infrequently, are the nose cone and two side shields of the satellite.

Initially, the period of revolution of *Sputnik* 3 was 105·98 min. and the orbital eccentricity 0·111. The height above the Earth varied between 122 n.miles (226 km.) at perigee and 1,014 n.miles (1,879 km.) at apogee, with perigee occurring when the satellite was going north at a latitude of 50° N. Though *Sputnik* 3 and its rocket began in almost identical orbits, they were soon separated by the action of air drag, which had a much greater effect on the rocket than on the denser instrumented cone. Fig. 1 shows the period of revolution of the cone (curve *A*) and the rocket (curve *B*), with values of orbital eccentricity marked on the curves. The total life-time of the rocket is likely to be rather less than seven months, whereas that of the instrumented satellite is expected to be about twenty-one months.

Though the rocket is due to make its final descent through the atmosphere early in December, its exact date of descent cannot be confidently predicted, be-

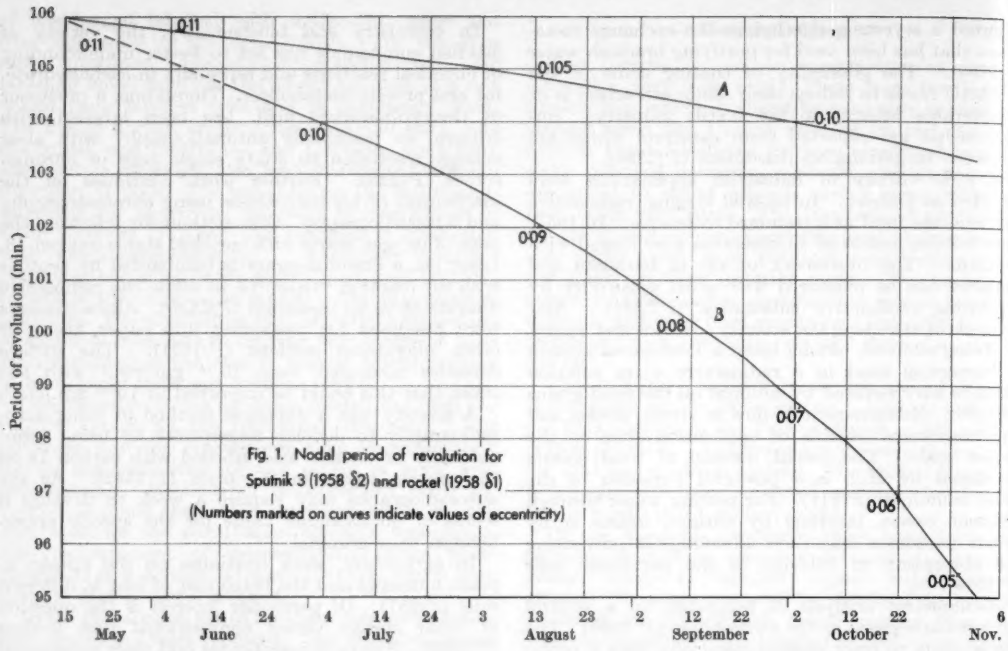

Fig. 1. Nodal period of revolution for Sputnik 3 (1958 δ2) and rocket (1958 δ1)
(Numbers marked on curves indicate values of eccentricity)

cause the period has been decreasing in an irregular manner. The daily change in period, instead of increasing smoothly, has behaved more like a step-function: the change was about 2·4 sec./day from June 20 to July 20, about 3·2 sec./day from July 31 to August 19, about 4·0 sec./day from August 23 to September 22, about 4·8 sec./day from September 24 to October 10, and about 7·4 sec./day from October 19 to November 5. The daily change in period of the instrumented satellite has also exhibited sharp variations, though these are not so well charted, because observations have been fewer and the irregularities smaller: the change in period was about 0·7 sec./day initially and had risen to 1·1 sec./day by October 20.

An irregular decrease in period implies irregularities in either the effective cross-sectional area of a satellite or the effective air density near perigee. If, as is likely, irregularities in air density are occurring, does the density depend on latitude, on a parameter dependent upon time, or on some other influence? Comparison of *Sputnik* 3 and its rocket suggests that the density is more likely to be varying with latitude than with time[1]; but there is, as with[2] *Sputnik* 2, some indication of an oscillation having a period of about twenty-seven days, which might be attributed to lunar tides; and solar disturbances may have some influence[3].

The rocket has been a bright object in the night sky, occasionally reaching stellar magnitude − 2 on favourable transits. Because it is rotating, its brightness has fluctuated greatly, sometimes by a factor of more than 100. The period of the fluctuations has shown a slow increase, from 8·5 sec. in mid-July to 9·0 sec. at the end of August and 9·5 sec. at the end of October. The instrumented satellite is, as its designation 1958 δ 2 implies, less bright than the rocket, and observers have found it fickle in its

Table 1. Orbital Data for *Sputnik* 3 (1958 δ 2)

Date 1958	May 15·3	July 4·0	Aug. 23·0	Oct. 12·0	
Nodal period (min.)	105·975	105·365	104·665	103·795	± 0·005
Semi-major axis (n.miles)	4003·1	3987·7	3970·1	3948·0	± 0·2
Eccentricity	0·1114	0·1080	0·1043	0·0995	± 0·0005
Perigee distance (n.miles)	3557	3557	3556	3555	± 2
Angle from apex to perigee	− 32°	− 49°	− 67°	− 85°	± 1°
Inclination to equator	65·19°	65·18°	65·17°	65·16°	± 0·04°

Table 2. Orbital Data for *Sputnik* 3 Rocket (1958 δ 1)

Date 1958	June 20·0	Aug. 4·0	Sept. 18·0	Nov. 2·0	
Nodal period (min.)	104·480	102·580	99·825	95·500	± 0·005
Semi-major axis (n.miles)	3965·4	3917·2	3846·7	3734·8	± 0·2
Eccentricity	0·1032	0·0925	0·0766	0·0506	± 0·0005
Perigee distance (n.miles)	3556	3555	3552	3546	± 2
Angle from apex to perigee	− 45°	− 61°	− 79°	− 97°	± 1°
Inclination to equator	65·17°	65·15°	65·12°	65·08°	± 0·04°

Notes: Apex is point of maximum latitude north. 1 n.mile = 6,080 ft. = 1·853 km. Last column gives estimated root-mean-square errors. No observations of 1958 δ 1 were made from Britain until mid-June.

behaviour: on some favourable transits it has remained obstinately invisible; at other times it has unexpectedly declared itself with flashes of stellar magnitude 1. It has not been necessary to rely entirely on optical observations, however, since the satellite has been transmitting radio signals on 20·005 Mc./sec., and these have, so far, continued with little diminution in strength.

Tables 1 and 2 give information on the orbits of *Sputnik* 3 and its rocket. The orbital inclination, like that[4] of *Sputnik* 2, has been decreasing slightly, probably as a result of lateral aerodynamic forces created by rotation of the atmosphere.

I wish to thank all those who have sent us observations of *Sputnik* 3 and its rocket, and Mrs. D. M. C. Walker, who has analysed the observations.

[1] King-Hele, D. G., and Walker, D. M. C., *Nature*, **182**, 860 (1958).
[2] King-Hele, D. G., and Leslie, D. C. M., *Nature*, **181**, 1761 (1958).
[3] Nonweiler, T. R., *Nature*, **182**, 468 (1958).
[4] Merson, R. H., and King-Hele, D. G., *Nature*, **182**, 640 (1958).

OBITUARIES

Prof. J. A. Gunn, C.B.E.

NEWS of the death on October 21 of J. A. Gunn in his seventy-seventh year will have been received with sorrow by a wide circle of friends and by all pharmacologists who knew him.

Gunn was a true pharmacologist, not a physiologist in disguise; that is to say, his primary interest was in the physiological effects which chemical substances foreign to the animal economy, whether synthetic or of plant origin, produce in animals. This interest led him to ponder deeply upon some of the problems presented by what we now call the structure – action relationships of drugs. In this he was probably influenced by his teacher, Sir Thomas Fraser, who, with his chemical colleague Crum Brown, had made the first systematic attempt to study the structure – action relationships of drugs. It was with Fraser that one of Gunn's earliest papers on "Venoms" was published. At the same time, in the true Scottish tradition, Gunn never forgot the therapeutic possibilities of the substances which he happened to investigate.

Gunn's general point of view was clearly stated in a short review, published in 1935, of his work on the alkaloids of *Peganum harmala*; this paper not only reveals his philosophy as a pharmacologist but is also an excellent example of his lucid and elegant prose style. He was the acknowledged authority on the pharmacology of the harmine alkaloids, on the study of which he was engaged intermittently for twenty-five years. When he began this work the structures of these alkaloids were unknown, but the brilliant investigations of W. H. Perkin, jun., and of Sir Robert Robinson eventually solved the structural problems, and Gunn profited from this work by receiving from Sir Robert Robinson several new and interesting derivatives of the natural alkaloids.

Gunn was the first professor of pharmacology to be appointed in the University of Oxford, and later became the first director of the Nuffield Institute for Medical Research. It is of some interest that he was convinced that every department of pharmacology ought to have a chemist on its staff. For a few years he was fortunate in having an able young chemist, Dr. C. J. Virden, in his Department, and the result of their collaboration was a series of papers on sympathomimetic amines. Gunn was the first to study the pharmacological effects of alkylating the phenolic groups of *para*- and *meta*-hydroxy- and 3 : 4-dihydroxy-phenylalkylamines. Even more interesting was his observation that the replacement of the β-methylene group of phenyl-ethylamine and -*iso*propylamine by an ethylene unit of structure scarcely altered, either qualitatively or quantitatively, the pharmacology of these bases.

Apart from his teaching and research activities, Gunn edited several editions of Cushny's great monograph on pharmacology after the latter author's death; he also wrote an admirable short book on pharmacology from which many generations of medical students have profited; the last edition, in which J. D. P. Graham collaborated, appeared shortly before his death. He was also for many years a member, and later chairman, of the Pharmacopœia Revision Commission, an arduous duty which he took very seriously. British pharmacology owes him a debt of gratitude, not least because the young, but flourishing, British Pharmacological Society owes its origin to his suggestion. Finally, his unselfish nature led him to take a great interest in the careers of young men, and there must be many well-established pharmacologists to-day who owe much to his encouragement and help, and who will remember him with affection and respect.

H. R. ING

Prof. Stanisław Loria

THE death on August 8 of Stanisław Loria is a great loss to Polish physics. He was one of the older generation of physicists, who knew well almost all the great men of the first half of our century. He knew Lorentz and Ehrenfest, and studied with Born and Ladenburg in Breslau. (Usually Prof. Born's first words to me, whenever we met, were: "How is Loria?") He worked in Manchester under Lord Rutherford, and during 1923–26 was a research associate in Pasadena, where he had been invited by Prof. R. A. Millikan. He was well acquainted with the old centres of research. It was a delight to hear him talking about his great teacher Witkowski, about Smoluchowski and Natanson, professors of physics in the old Jagellonian University of Cracow, about Madame Skłodowska Curie, about all the great physicists whom he knew personally and whom the present generation know only from the literature.

Stanisław Loria was born in 1883 in Warsaw. He went to high school and took his university degree in Cracow. In this former Polish capital, then a part of the Austrian Empire, the Polish language was not banned either from the high schools or from the University. There he received his Ph.D. and went for further studies to Wrocław (then Breslau), Göttingen and Berlin, where he spent the years 1907–10. At this time, with Ladenburg, he discovered the phenomenon of anomalous dispersion in hydrogen; the first note on this important effect appeared in *Nature* in 1908.

In 1910 he became a reader (*docent*) in physics in the University of Cracow and in 1919 a professor of physics in the University of Lwów. There he remained until the Second World War—with long

intervals devoted to research in laboratories abroad. Even through the War he was in Lwów—up to 1941, when the Germans occupied the town. His last work before the War concerned the problem of diffraction of electrons with energies between 18,000 and 4,500 volts. Unfortunately, it was only partially published, since the apparatus and notes were taken away or destroyed by the Nazis. Prof. Loria had to hide during the German occupation. In free Poland he was a professor in Wrocław and later in Poznań. He died in a London hospital, where he had undergone an operation.

During his life Prof. Loria was very much interested in theoretical physics; he was one of the first physicists who studied Einstein's paper of 1905 and, some years later, wrote in his vivid style a book on relativity theory, the first that appeared on this subject in Poland.

Prof. Loria will be remembered by many Polish physicists. Some of them, including the present writer, owe to his encouragement and help the beginning of their academic careers.

Leopold Infeld

Mr. E. W. Swanton, O.B.E.

Mr. Ernest William Swanton died at Twickenham on October 21 at the age of eighty-eight. After spending his early years as a schoolmaster and private tutor, Swanton was in 1897 appointed the first curator of the Educational Museum at Haslemere, which had been established in 1888 by Mr. (later Sir) Jonathan Hutchinson, a well-known London surgeon. Hutchinson had many novel ideas on the value and arrangement of museums for educational purposes, particularly in the use of living material, the open display of specimens so that they could be handled and in making objective teaching "within the easy ken of all ordinary minds". It was Swanton who was mainly responsible for putting Hutchinson's ideas into practice, and so successfully did he build up the educational work that S. F. Markham, in his "Report on the Public Museums of the British Isles", was able to say in 1938: "At Haslemere possibly more educational work of this kind is done than in any comparable museum centre in the country".

In 1898, a few months after his appointment as curator, Swanton began to give regular series of lessons in natural history to children from the local elementary schools, illustrating his lectures by handing around specimens from the Museum collections—an early, if not the earliest, use of museums by organized parties of school-children in this way, and a tradition that has been continued at Haslemere to the present time. In 1899, Swanton organized another feature originated by the founder, which he continued throughout his curatorship: a museum examination for individual local children in which, after several months preparation in the museum galleries in their own time, they were called upon to answer an examination paper covering the whole scope of natural and human history. This was widely hailed as a new contribution to museum teaching techniques.

Swanton had wide antiquarian and natural history interests, but he will be remembered chiefly as a field mycologist. In 1898 he was a foundation member of the British Mycological Society and became its president in 1916. The Society had many notable forays in the Haslemere district with Mr. and Mrs. Swanton as genial hosts. In 1909 he published a useful popular handbook, "Fungi and how to Know Them", which had a second edition in 1922. Among his other publications were "A Pocket Guide to the British Non-Marine Mollusca" (1906), "British Plant Galls" (1912), "A Country Museum" (1947) and, jointly with P. Woods, "Bygone Haslemere" (1914). In the last year of his life he wrote and had privately printed three small books, "A Brief Autobiography", "The Yew Trees of England" and "Memories and Notes".

Swanton was elected an associate of the Linnean Society in 1920, and in 1936 his work at the Museum was recognized by his appointment as M.B.E.; he was advanced to O.B.E. in 1948, the year when he retired. In 1949 he was granted a Civil List pension. His wife, whose help in the work of the Museum he frequently acknowledged, died in 1957.

John Clegg

NEWS and VIEWS

Royal Medals of the Royal Society

H.M. The Queen has been graciously pleased to approve the recommendations made by the Council of the Royal Society for the award of the two Royal Medals for 1958 as follows: to Prof. H. S. W. Massey, Quain professor of physics at University College in the University of London, for his distinguished contributions to physics, and particularly for his experimental and theoretical studies of collision phenomena in gases; to Prof. A. L. Hodgkin, Royal Society research professor, for his distinguished work on the mechanism of excitation and conduction in nerve and muscle.

Directorship of Dunsink Observatory: Dr. M. A. Ellison

Dr. Mervyn A. Ellison, principal scientific officer at the Royal Observatory, Blackford Hill, Edinburgh, since 1947, has been appointed senior professor of astronomy at the Dublin Institute of Advanced Studies and director of the Dunsink Observatory, situated a few miles from Dublin. Dr. Ellison spent his early years in Ireland, first in the south where he was born in 1909, and later at Armagh Observatory, where his father, Canon W. F. A. Ellison, well known for his astronomical optical work, was director during 1918–36. After graduating at Trinity College, Dublin, in 1932, he taught for some years at Sherborne and successfully pursued his study of solar phenomena in his leisure time, until his appointment at Edinburgh enabled him to devote himself completely to this work. He has published a series of papers on solar flares and their terrestrial effects and on stellar scintillation, which have brought him international recognition, and is the author of a well-known book on "The Sun and Its Influence", which has been translated into several languages, including Russian. He is popular as a lecturer and broadcaster and is president of the Astronomical

Society of Edinburgh. Dr. Ellison is correspondent for solar activity of the British National Committee for the International Geophysical Year and has just been elected to succeed Dr. Y. Öhman, of Sweden, as international reporter for solar activity. After the death of Prof. W. M. H. Greaves and until the appointment of Prof. H. A. Brück as his successor (see *Nature*, **179**, 454; 1957), Dr. Ellison served for nearly two years as acting director of the Royal Observatory, Edinburgh. He now succeeds Prof. Brück in the post at Dunsink.

A Commonwealth Overseas Research Council

Lord Home, Secretary of State for Commonwealth Relations, announced at the Commonwealth Trade and Economic Conference in Montreal on September 24 that an Overseas Research Council is to be established to aid Commonwealth countries in scientific research. The United Kingdom Research Councils —Department of Scientific and Industrial Research, Medical Research Council and Agricultural Research Council—are willing, he said, to provide advice and assistance on research matters falling within their respective fields to any Commonwealth country requiring such assistance, wherever this can be done within the funds available. The Overseas Research Council will provide for the co-ordination of this assistance. It will advise Ministers on questions of co-operation in scientific research overseas and will also provide a central point to which Commonwealth Governments and research institutions can refer for advice and information.

The International Atomic Energy Agency: Scientific Advisory Committee

The Board of Governors of the International Atomic Energy Agency has appointed the following to serve on the Agency's Scientific Advisory Committee: Prof. H. J. Bhabha (India) (subject to the concurrence of the Government of India); Sir John Cockcroft (United Kingdom); Prof. V. S. Emelyanov (U.S.S.R.); Prof. B. Goldschmidt (France); Prof. B. Gross (Brazil); Prof. W. B. Lewis (Canada) and Prof. I. I. Rabi (U.S.A.). The function of this Committee is to provide the Board and the Director-General of the Agency with advice on scientific and technical questions arising out of the Agency's programme. The members are appointed in their personal capacity, with the concurrence of their respective governments. Membership of the Committee is identical with that of the Scientific Advisory Committee of the United Nations, and it is expected that this fact will still further strengthen the relationship between the International Atomic Energy Agency and the United Nations.

Nuclear Safety Advisory Committee

In moving the second reading of the Nuclear Installations (Licensing and Insurance) Bill in the House of Lords on November 13, the Minister of Power, Lord Mills, said that he and the Secretary of State for Scotland had decided to appoint a Nuclear Safety Advisory Committee composed of experts of the highest standing. They regarded such a Committee as necessary in view of the rapid strides which nuclear science and engineering were making and the consequent continuous evolution of the attendant problems of safety. In making appointments to the Committee, they intended to consult, *inter alia*, the Atomic Energy Authority, manufacturers of nuclear plant, the insurers, and the owners and operators of major nuclear installations. They had decided to establish this Committee administratively rather than by statute because developments in the industry were hard to foresee and might eventually necessitate changes in the constitution of the Committee or its terms of reference and such changes would thereby be more easily made. Referring to the exemption of the Atomic Energy Authority from licensing under the Bill, Lord Mills explained that the Authority's work was mainly experimental. To include it, apart from involving delays, would require a much larger inspectorate and also inspectors as expert in advanced research as the Authority's own scientists. Government departments would not normally be subject to licensing, but it was intended that they should follow the safety principles evolved between the Minister, the Atomic Energy Authority and the Nuclear Safety Committee and they would be under the same third-party liability as the Authority. Replying to questions in the debate, Lord Mills added that the Bill did not cover the question of hospitals or the manufacture of pharmaceuticals, nor was it intended to cover ordinary university research or similar activities. If and when these activities required cover, fresh measures would be laid before Parliament.

Moon Rocket Tracking

A 108-mc./s. interferometer with a base line of 80 wave-lengths was used by the Royal Aircraft Establishment of the Ministry of Supply on November 8 to track the third American Moon rocket. A satisfactory record was obtained during 07.47–08.01 G.M.T., that is, for the time the rocket was above the horizon as seen from Great Britain. When the complete analysis is available the bearing of the rocket from Lasham, Hampshire, where the interferometer is located, will be known at every instant during this period with an accuracy of about 1 sec. of arc—an accuracy in position of approximately 10 miles at 4,000 miles range. Since the launching point is known, it should be possible to determine the complete orbit of the rocket, and by extrapolation to make a very fair estimate of the area where any surviving pieces may be. It is interesting to note that observers at Lasham realized at 07.55 that the missile had gone astray, since the type of record obtained was similar in character to those for the American Earth satellites. It is a feature of this equipment that a rapid assessment of the missile projectory is possible. The accuracy of bearing realizable with a fixed aerial equipment of this type is some hundred times greater than is possible with types of steerable aerials.

Central Agency for Carbon-14 Determination

During recent years, the study of primary production in the sea has been followed by radioactive tracer methods using carbon-14, a technique first employed by Nielsen. The method is very useful in that the field-work does not presuppose any expert knowledge of radiochemistry. On the other hand, manufacture of the necessary ampoules of sodium bicarbonate solution labelled with carbon-14, and the measurements of the radioactivity of the resulting filters, do require the facilities of a well-equipped radiochemical laboratory. In order to make such facilities available to the smaller marine laboratories, the recommendations adopted at the 1957 Bergen symposium on "Measurement of Primary Production in the Sea" have now been implemented and a central agency has been set up at Charlottenlund Slot, Denmark. This has been made possible by the

provision of funds by Unesco in January 1958, and of a room in its residence at Charlottenlund Castle by the Danish Institute for Fisheries and Marine Research. Prof. E. Steemann Nielsen, adviser in plankton research for that Institute, has been appointed honorary supervisor, and the daily work will be directed by Mr. Vagn Hanson, also of the same Institute. The facilities of the Agency are available to all scientific institutions in the world, and as well as providing the service mentioned above, the Agency also supplies the necessary ancillary equipment for use in the field. Full details can be obtained from Prof. E. Steemann Nielsen, The International Agency for Carbon-14 Determination, Charlottenlund Slot, Charlottenlund, Denmark.

British Information Services

Questions in the House of Commons on November 3 regarding the improvement of British information services overseas brought a reply from the Chancellor of the Duchy of Lancaster, Dr. Charles Hill. He said that as a result of his visit in September to information posts in India, Pakistan, Aden, British Somaliland, Kenya, Ethiopia and Somalia, he had formed the conclusion that we should intensify our effort, adapt it to new circumstances and increase the resources available. He referred particularly to the need to counter hostile radio propaganda, to increase the flow of British books, and to expand the programme of teaching English. The Government has approved in principle a substantial strengthening of our information effort, and plans are now being worked out. He hoped to report in detail in a few weeks time, and in reply to a further question promised to consider the issue of a White Paper showing the progress made in implementing earlier proposals. That relating to the distribution of English books overseas was particularly welcomed.

High-Altitude Research

In reply to questions in the House of Commons regarding Earth satellites on November 3, the Minister of Supply, Mr. Aubrey Jones, said that the *Black Knight* is a test vehicle for high-altitude research, and a programme of further firings is planned. The opportunity for space research arises from certain techniques being developed for the defence programme. His officials are in constant touch with the Office of the Lord President of the Council and numerous scientific authorities on the scientific value to be obtained from British participation in space research, including research investigations by satellites. The scientific value and not finance is the real question at issue, and the possibility of co-operation with other countries is also taken into account.

Salaries of Teachers in Technical Institutions

One of the main recommendations of the committee which, under the chairmanship of Sir Willis Jackson, met to consider the supply and training of teachers for technical institutions was the need to recruit people of good calibre from industry. Perhaps the greatest deterrent is the disparity between the salaries paid to technical college teachers and their colleagues in industry. This matter has been considered recently by the Association of Teachers in Technical Institutions, leading to a memorandum which has been submitted to the Teachers' Panels of the Burnham Main Committee and the Burnham Technical Committee.

The main recommendations include the abolition of all grade *A* assistant posts in technical institutions and that all teachers holding these positions should become assistants grade *B*; this grade should be renamed 'assistant lecturer'. The remaining grades of teacher should remain substantially as at present except that the grade of 'reader' should be renamed 'principal lecturer' and be available for research, advanced teaching or administrative responsibility in all colleges doing work of university standard. A new grade of deputy head of department should be established for large departments. For all these grades there should be increases in salary in appropriate relation to the increases given to assistant lecturers. The Association also proposes the establishment of national scales of salaries for part-time teachers, based on the principle that the cost of carrying a given teaching load should be the same whether the work is done by part-time or full-time teachers.

Unesco Programme for Arid Lands

Unesco Information Manual 3 contains a concise, clear and readable account of the Unesco Programme for Arid Lands (pp. 31. Paris: Unesco; London: H.M. Stationery Office, 1958). Commencing with a statement of the nature and extent of the problem presented by the arid zones, representing about one-third of the Earth's total land surface of 33,000 million acres, compared with the 3,300 million acres under cultivation, the pamphlet briefly describes the way in which the problem has been attacked by Unesco during the past ten years, its search for facts, the steps taken to inform the scientific world, through, for example, a Directory of Institutions engaged in Arid Land Research and a Guide Book to Research Data for Arid Land Development, and the way in which the attack on the desert has now become a major project of Unesco. Steps taken to develop water resources are indicated, including the use of artificial means for provoking rainfall, demineralization of salt water, studies in plant ecology of the arid zone, and the harnessing of sun and wind, and the pilot project to study the social adjustment of nomadic and semi-nomadic groups to settled existence. An outline is given in the 1957–58 programme. The pamphlet contains a bibliography and a select list of visual aids on a subject in which, besides the International Council of Scientific Unions and several of the individual unions, the Scientific Council for Africa South of the Sahara, the World Power Conference and a number of other international bodies are already interested.

The Analyst

The earliest ten volumes of *The Analyst*, for the years 1876–85, have been re-published in facsimile form by W. Heffer and Sons, Ltd., of Cambridge, who are the publishers of the journal on behalf of the Society of Analytical Chemistry. These volumes cover the early years of the operation of the Sale of Food and Drugs Act, 1875, and are of considerable historical importance. During these ten years chemical analysis passed from the sphere of the dilettante chemical investigator to that of an exact science, capable of legal argument and applicable on an industrial scale. The analysis of water was systematized, and the beginnings of biological examination are described in many of the papers. The Society whose journal this is, although then named 'The Society of Public Analysts', has catered from its inception for all

classes of analyst; for example, Vol. 1 contains papers on the analysis of coal and of plating and gilding solutions, as well as much work on various foods. Each volume is available separately from any bookseller or direct from the publishers at 6 guineas, bound in cloth boards in the style of the original. Publication in America is through the Johnson Reprint Corporation.

The Wellcome Museum of Medical Science

Since it was opened by the Wellcome Foundation in 1914, the Wellcome Museum of Medical Science in Euston Road, London, has provided a unique display of photographs, specimens and extracts from medical literature, which give, in study units housed in comfortable and attractive bays screened off from the rest of the Museum, comprehensive information about each of the diseases dealt with (see "The Wellcome Museum of Medical Science". Pp. 40. London: The Wellcome Foundation, Ltd., 1958). Some 10,000 doctors, nurses, medical missionaries and students visit the Museum each year from all parts of the world. Originally the Museum was devoted largely to tropical diseases, but nowadays it covers a much wider field. Recently reorganized, it now reflects the changes in emphasis on certain diseases which have resulted from the remarkable advances in control and treatment that have been made in recent years. Thus, the thirty-two panels formerly given to syphilis have now been reduced to four, and the seven panels given earlier to plague have been reduced to three. Cholera also is no longer feared as it used to be. Malaria, however, still occupies forty-two panels, though if the schemes for its control and eradication continue to succeed as they have done during the past five years, much less space will be needed to cover this disease, which has for long been the greatest single cause of illness and death in the world. Tuberculosis, on the other hand, is likely to be given more space to illustrate its importance in the tropics. A pleasing feature of the Museum's activities is the use that is made of it by boys' and girls' schools, to which the Museum lends suitable selections of material for the stimulation of interest in biology. It also lends or gives exhibits to medical schools throughout the Commonwealth. Last year a section of the Museum was shown in Durban, South Africa, and another section, devoted to trypanosomiasis in Africa and South America, was shown at the sixth International Congress on Tropical Medicine and Malaria at Lisbon.

Systematics of Parrot-fishes

The brightly coloured parrot-fishes are ubiquitous denizens of coral reefs throughout the tropics. For feeding on coral the dentition has been greatly modified, with fusion of the teeth in the front of the jaws into a pair of dental plates forming the 'parrot's beak' from which these fish get their name. The pharyngeal musculature is highly developed and operates a mill formed of grinding teeth on the pharyngeal bones. Many of the species have a large swelling on the forehead which adds to their bizarre appearance. In the past, the systematic description of this group has been highly confused and more than 350 species have been named and described. In a recent publication (U.S. National Museum, Bulletin 214: Review of the Parrotfishes, Family Scaridae, by L. P. Schultz. Pp. v+143+27 plates. Washington, D.C.: Government Printing Office, 1958. 75 cents), the curator of fishes of the United States National Museum has done much to unravel the confused systematics of the parrot-fishes. He claims that only eighty species can be regarded as valid. Many of the large number described, he points out, have been erected into so-called species on the basis of colour patterns which vary not only between individuals but between different stages in the life-history of one individual, while there is also a sexual dichromatism. His review of the Scaridae at last places this family in some sort of perspective and demonstrates their relationship with the labrid fishes. There are excellent keys to genera and species.

Dormancy in *Viburnum* Seeds

In an investigation of dormancy in the seeds of *Viburnum trilobum*, R. H. Knowles and S. Zalik (*Canadian J. Bot.*, **36**, 561; 1958) have observed this phenomenon in seedlings as well as in seeds. When seeds were maintained at 20° C. under suitable conditions for germination, there was slow growth in the radicle and hypocotyl in some seeds, while others showed no response. They have found that this kind of dormancy is associated with the presence of a water-soluble inhibitor in the endocarp and with the need for an appropriate (inductive) temperature treatment prior to exposure to a constant 20° C.; they also found that dormancy in the epicotyl, namely, failure of shoot growth in the young seedling, could be overcome by removing the cotyledons.

Tropical Karst

Landforms developed in regions of massive limestone or dolomite where erosion is principally by solution of the rock rather than mechanical corrasion have long been known as 'karst' from the area in Yugoslavia where they were first investigated. The karstlands of temperate latitudes have received considerable attention, but their occurrence in tropical areas has been less closely studied. In an article in the *Geographical Journal* (**124**, part 2, 184; June 1958) Dr. Marjorie Sweeting gives an admirably lucid account of its distribution and characteristics in Jamaica. She shows that even in an area of pure, free-draining limestone an annual rainfall of 100 in. or more is sufficient to maintain a heavy forest cover and that water passing through this cover is so highly charged with organic carbon dioxide that the solution rates may be 400 per cent greater than in cooler climates. The most characteristic land-form produced under these conditions is 'cockpit karst', in which the entire surface is covered by conical depressions, here 300–400 ft. deep, separated by cone-like hills. There are no watercourses on the surface. Where the crystalline white limestone passes into other formations and free vertical drainage is checked, solution and sapping takes place along the base and sides of the cockpits and the mechanical effect of flood water in undercutting and steepening the sides is considerable, and 'tower karst' develops. Dr. Sweeting indicates that in areas of more marly limestone and lower rainfall dolines and poljes, already well known from European examples, develop. She gives some attention also to associated caves and underground river systems.

Mond Nickel Fellowships

The Mond Nickel Fellowships Committee recently announced the award of fellowships for 1958 to the following: Mr. G. H. Longworth (Lancashire Steel Manufacturing Co., Ltd.) to study the manufacture of plain carbon and alloy steels for rod and wire

products in the United Kingdom, on the Continent, and in the United States; Mr. J. C. Morrison (Carron Company) to study melting, moulding and heat treatment of alloy cast irons, quality control of metal and sand plants in modern foundries, and new developments in related metallurgical processes; Mr. T. Tait (Colvilles Limited) to study the technical and economic factors involved in the use of oxygen in steel industries in the United Kingdom, on the Continent, and in the United States and Canada.

The Mond Nickel Fellowships Committee is offering one-year fellowships valued at £900–£1,200 for 1959, to graduates of British nationality to enable them to obtain wider experience and additional training in industrial establishments, in Britain or abroad, to make them more suitable for future employment in senior technical and administrative positions in British metallurgical industries. Applicants will be required to state details of the programme they wish to carry out. Particulars and forms of application are available from the Secretary, Mond Nickel Fellowships Committee, 4, Grosvenor Gardens, London, S.W.1.

Mechanization of Thought Processes

A SYMPOSIUM on "The Mechanization of Thought Processes" is being held at the National Physical Laboratory, Teddington, during November 24–27. More than two hundred delegates will be attending. After opening sessions on general principles, succeeding sessions will be devoted to automatic programming, language translation, speech recognition, learning in machines, and implications for biology and for industry. Further information can be obtained from the Chief Information Officer, Department of Scientific and Industrial Research, Charles House, 5–11 Regent Street, London, S.W.1.

United Nations Conference on Peaceful Uses of Atomic Energy: Proceedings

THE United Nations have announced that the pre-publication period for the Proceedings of the Second U.N. International Conference on the Peaceful Uses of Atomic Energy, during which complete sets may be ordered at a special price, has been extended to January 31, 1959. The action was taken to facilitate the budgetary arrangements of institutions unable to purchase the complete set of volumes from their 1958 budgets. Until January 31, the thirty-three volumes of the English edition may be ordered for 435 American dollars, £155 sterling, or 1,860 Swiss francs. The special pre-publication price for the complete set represents a saving of some 70 dollars as compared with the regular price of the set. For the French and Spanish editions, each of which is expected to include approximately fifteen volumes, the special pre-publication price will be 190 U.S. dollars, £68 sterling, or 815 Swiss francs. If the number of volumes is less than fifteen, proportionate refunds will be made to subscribers who have ordered a full set. Further information can be obtained from the United Nations, Sales and Circulation (Atomic Energy), United Nations, New York.

The de Havilland Aircraft Co., Ltd.: Appointments

MR. R. G. MCCOY has been appointed general manager of the de Havilland Aircraft Co., Ltd., with effect from December 1. He joined the company in May 1953 as deputy service manager, becoming manager in April 1954, and was responsible for the Service Department until July 1958, as well as acting as assistant to the managing director from January 1956. Mr. D. R. Newman has been appointed chief aerodynamicist of the company with effect from December 1. Mr. M. Herrod-Hempsall remains responsible for administration in the Aerodynamics and allied Departments. Mr. Newman joined the de Havilland Aeronautical Technical School in April 1936 and has been in the Aerodynamics Department since May 1938.

Announcements

PROF. E. E. ZEPLER, professor of electronics in the University of Southampton, has been elected president of the British Institution of Radio Engineers for 1958–59.

SIR WALTER DRUMMOND has been appointed chairman of the Farm Buildings Research Committee of the Agricultural Research Council, in succession to Lord Rothschild. The Farm Buildings Research Committee has been set up by the Council to co-ordinate the different research activities concerned with farm buildings and to advise on their further development.

THE 125th meeting of the American Association for the Advancement of Science will be held in Washington, D.C., during December 26–31, with headquarters in the Sheraton-Park Hotel. In addition to the eighteen sections of the Association, about ninety-two affiliated and associated societies will participate. The presidential address, on "Fifty Years of Medical Genetics", will be delivered by Dr. Laurence H. Snyder, president of the University of Hawaii, and retiring president of the Association. Further information can be obtained from Sidney S. Nagus, Medical College of Virginia, Richmond, Virginia.

A GROUP of experts from Australia, Germany, Iran, Portugal, South Africa, United Kingdom and the United States is meeting, under the auspices of the Food and Agriculture Organization and the Office International des Epizooties, to consider problems of ticks and tick-borne diseases. The meetings are being held during November 24–29, at the Royal College of Veterinary Surgeons in London. Further particulars can be obtained from the Registrar of the College, 9 and 10 Red Lion Square, London, W.C.1.

THE 129th course of six Christmas lectures "adapted to a juvenile auditory" will discuss the International Geophysical Year, and is to be delivered at the Royal Institution on December 30, 1958, and January 1, 3, 6, 8 and 10, 1959, at 3 p.m. The lectures are as follows: "The Ionosphere and the International Geophysical Year", by J. A. Ratcliffe; "Geomagnetism", by J. M. Stagg; "Exploration of the Upper Atmosphere", by Dr. R. L. F. Boyd; "Meteorology", by Sir Graham Sutton; "Oceanography in the International Geophysical Year", by Dr. G. E. R. Deacon. Applications for tickets (juveniles, aged 10–17, £1; adult non-members, £2) should be addressed to the Royal Institution, 21 Albemarle Street, London, W.1.

A SYMPOSIUM on "Experimental Approaches to the Problems of Growth and Form in Plants" is being held in the rooms of the Linnean Society of London during December 19–20. This is being arranged by the Experimental Plant Morphology Group of the Society and the Symposium is open to visitors. Further information can be obtained from the Secretaries, Linnean Society, Burlington House, Piccadilly, London, W.1.

THE WORLD REFERENCE LABORATORY FOR FOOT-AND-MOUTH DISEASE

THE control of diseases of livestock is an important feature in the general economy of most countries in improving animal production and in fostering international trade in livestock and animal products. Foot-and-mouth disease is one of the most troublesome of the infectious diseases of livestock, and increasing attention is now being given on an international basis to its control and eradication.

It is gratifying to learn in this connexion that one of the recent steps taken, following negotiations between the Food and Agriculture Organization of the United Nations and the British Government, has been the establishment of a World Reference Laboratory for Foot-and-Mouth Disease at the Research Institute (Animal Virus Diseases), Pirbright, Surrey, which functions administratively under the ægis of the Agricultural Research Council.

It is particularly appropriate that the Pirbright Institute should have been asked to accept this responsibility because of its experience in the examination of virus material from all over the world during the past ten years and because it has all the necessary facilities for the full examination of suspect material.

The Institute reported recently the results of the examination and immunological classification of 2,200 virus samples from outbreaks in countries in Europe, Africa, Asia and the Americas. This must be considered only as a useful first contribution to a very big epizootiological problem as there are many areas which have not yet been covered. A satisfactory epizootiological world picture cannot be produced until a reasonably large number of samples have been examined from outbreaks in as many countries as possible. The Food and Agriculture Organization is seeking the co-operation of governments so that the surveys carried out for a number of countries will be continued and extended. It is hoped that one of the immediate results of this will be the continued collection and dispatch to the World Reference Laboratory, now established, of suitable field samples from outbreaks of the disease in countries all over the world.

The virus of foot-and-mouth disease, unlike those of yellow fever and rinderpest, is characterized by the lack of antigenic homogeneity. There are at present seven main immunological types of the virus (compared with three in poliomyelitis, three in influenza, three in equine encephalomyelitis and two in vesicular stomatitis). The well-known types *O*, *A*, and *C* (1922–26) have been found in Europe, the Americas, Asia and Africa, and the work of the Pirbright Institute has brought to light four other types, three (*S.A.T.*1, *S.A.T.*2 and *S.A.T.*3) at present known only in Africa but one as far north as Egypt, and the fourth, *ASIA* 1, only in Asia but as far west as Iran and Israel. It is possible that other types of the virus may be discovered as the result of more extended surveys. There are, in addition, strains of the virus within each main immunological group which differ sufficiently in antigenic constitution to classify them as variants or sub-types. Control programmes in many parts of the world include vaccination, and an essential to make these effective is accurate information on types and strain differences, so that appropriate vaccines can be used.

It is universally recognized that there is considerable advantage in having a central laboratory which is in a position to collect information on the distribution of virus types responsible for outbreaks, sporadic, enzootic and epizootic, and to complete surveys by collecting essential information on the character of outbreaks, the number and species of animals involved, the possible origin of outbreaks and other relevant details. The resulting epizootiological picture would be of much value in organizing methods of control and eradication and in assisting countries to estimate risks associated with trade. Reports of the world position will be issued through the Food and Agriculture Organization from time to time.

The functions of the World Reference Laboratory will include also the examination and classification of virus types and sub-types, the ultimate establishment of a collection of all types and confirmed sub-types and their corresponding antisera. It is not intended that the World Reference Laboratory should undertake the routine examination of virus material from European countries or the Americas, since there are already facilities for this purpose. The World Reference Laboratory will, however, give all possible assistance if specially requested to do so and will be assisting with the sub-type classification problem and be responsible for the examination and identification of strains of virus suspected to be other than types *O*, *A*, and *C*.

THE NATIONAL VEGETABLE RESEARCH STATION

REPORT FOR 1956–57

THE eighth annual report* of the National Vegetable Research Station, recently published, provides a summary of the progress made by the eight sections of the Station. Some of our common vegetables are receiving the attention of the plant breeders, and further advance has been made in selecting a non-bolting type of red beet having single-seeded fruit. The production of onion and brussels sprout hybrids and a winter-hardy culinary pea is also being pursued. A report by L. E. Watts and R. A. T. George on a two-year investigation of the classification and performance of radishes involved the testing of 114 varieties made up of approximately equal numbers from British and foreign sources. An appendix to this report gives a classification and grouping of radish varieties. The authors conclude that there is no urgent need for a breeding programme for this vegetable as commercial varieties of satisfactory quality are already available.

* British Society for the Promotion of Vegetable Research. Eighth Annual Report, 1957 (October 1956–September 1957). Pp. viii+67. (Wellesbourne, Warwick: British Society for the Promotion of Vegetable Research, 1958.)

The Chemistry Section has continued the analysis of the long-term field experiments and investigated the effect of different manurial treatments on soil structure. An examination of the biochemical factors affecting the germination of seeds was commenced. The chemical changes occurring in the root of red beet when clamped and during flowering are being studied. The nature of the competition between weeds and vegetables is one of the problems being investigated in the Physiology Section, which is also concerned with growth studies of vegetable crops with the object of finding how various manurial treatments affect the growth and yield of crops. The influence of various treatments on the flowering of vegetables is being studied. In the Irrigation Section emphasis is shifting from treatments applied throughout the life of the plant to treatments applied at certain stages of growth. In general, it has been found that abundant water supply increases the quality of foliage of most vegetable plants and also increases the yield of saleable material. It seems clear that each crop will have to be considered on its merits regarding irrigation requirements. Work has continued on the development of an irrigation gauge.

The Entomology Section has made further studies on beetle predators of the cabbage root fly. It was confirmed that low rates of soil insecticides broadcast on the soil resulted in an increased infestation of cabbage root fly. Further work is being carried out on the soil application of soil insecticides for control of carrot fly on carrots and parsnips. An outstanding result obtained by the Pathology Section was the successful use of zinc frit for control of the crook root disease of watercress, resulting in increased yield. Weed investigations include observations on the effect of vegetable cropping on the weed population of original corn land. Various herbicide trials are also in progress. The Statistics Section has, besides handling routine inquiries from other Sections, investigated fitting of growth curves and has worked out designs for the assay of virus preparations on *Nicotiana glutinosa* and *Phaseolus vulgaris*. Apart from the usual weather observations, the use of a special rain-gauge with its rim only 1 in. above ground was continued. Rainfall collected in this gauge was 5 per cent greater than that collected in the standard gauge, thus confirming previous observations at this Station. By using gauges at different heights above the ground it was found that the amount of rain collected was a function of the height of the gauge above the ground and the run of the wind.

METALS AND ALLOYS ABOVE 1,200° C.

A SYMPOSIUM on "The Study of Metals and Alloys above 1,200° C." was held in the Department of Metallurgy of the University of Oxford on September 17 and 18; the subjects discussed at the four sessions are outlined below. Prof. W. Hume-Rothery welcomed the visitors to the symposium in an introductory address, and emphasized the increasing importance of the topic under discussion. He urged that metallurgists should look ahead five or ten years: design engineers were always limited by the high-temperature alloys available to them.

Metals and Alloys of High Melting-point

The first session was devoted to a study of the properties of some refractory metals and alloys—the platinum metals, tungsten alloys, molybdenum, and titanium–carbon alloys. Prof. E. Raub (Forschungsinstitut für Edelmetalle und Metallchemie) emphasized the relatively high reactivity with gases and refractory materials possessed by the platinum metals and alloys at high temperatures. Subsequent discussion centred on whether oxygen diffusion can take place through platinum, and it was concluded that it did not diffuse through metal of very high purity, although internal oxidation, for example, has been observed in dilute alloys. Raub also considered the reaction of the platinum metals with refractory materials, and described methods of melting and annealing these alloys, pointing out the main difficulties encountered by metallurgists studying their behaviour.

R. Kieffer, K. Sedlatschek and H. Braun (Metallwork Plansee, Reutte-Tirol) presented a paper on sintered high-melting tungsten alloys, outlining various methods for preparing the metal and for the production of cold ductile alloys. The alloy systems described were tungsten–molybdenum, tungsten–niobium and tungsten–tantalum; in the last case the following properties of sintered tungsten alloys with 0–100 per cent tantalum were outlined: density, hardness, elastic moduli, electrical resistivity, ease of hydrogenation, oxidation behaviour and corrosion resistance in acids and alkalis.

A. R. Moss (Armaments Research and Development Establishment, Woolwich) considered the thermal, mechanical and physical factors affecting the grain structure of arc-melted molybdenum, and finally R. L. Bickerdike and G. Hughes (Royal Aircraft Establishment, Farnborough) described a vacuum-quenching furnace which had been used to examine the titanium-rich end of the titanium–carbon system between 1,558° C. and 1,763° C.

High-temperature Techniques

The session opened with papers on zone melting by G. A. Geach and F. O. Jones (Associated Electrical Industries) and J. A. Belk (Woolwich). The first paper described an arc-melting technique and also a floating-zone method, using electron-bombardment heating to melt a narrow zone of the specimen, applied to refractory metals including rhenium and tungsten. Belk gave further details of the latter method, applied to the removal of carbon from vacuum-cast molybdenum. The mechanical properties of the purified material in single crystal and polycrystalline form were summarized.

Arc-melting processes were outlined in papers by A. R. Moss (Woolwich), J. R. Murray and G. K. Williamson (Atomic Energy Research Establishment, Harwell) and F. O. Jones, A. G. Knapton and J. Saville (Associated Electrical Industries). Moss discussed the basic principles of the various vacuum-arc and inert-gas arc-melting processes, followed by a consideration of the electrical and mechanical equipment in common use. Murray and Williamson reviewed the application of arc-melting, and other melting techniques used in alloy investigations at temperatures above 1,200° C. at Harwell, and further

descriptions of arc-furnace techniques were given by Jones, Knapton and Savill, who also considered electron bombardment heating as supplementary to arc-furnace techniques. Finally, a special molybdenum-wound cooling curve furnace was described by W. Oldfield (British Cast Iron Research Association), in which the element completely surrounds the specimen container.

Physical Properties and Equilibria at High Temperatures

The first two papers were concerned with crystal structure. A. J. Martin and A. Moore (Atomic Weapons Research Establishment, Aldermaston) discussed the structure of beryllium at temperatures between −185° C. and 1,290° C. No evidence was found to support other workers' claims of allotropy in the range 400–800° C. They showed, however, that the lattice is hexagonal up to about 1,250° C., above which the structure is body-centred cubic, and the authors discussed the possibilities of retaining this structure form at temperatures below 1,250° C.

The Metallurgy Department, Royal Aircraft Establishment, Farnborough, then presented a paper on the structures of graphites deposited from hydrocarbon gases at various temperatures and pressures. The effect of changes in deposition temperature on the density and X-ray diffraction pattern was shown. 'Flecks', not unlike deformation bands, are produced on the surface of these graphites when they are deformed.

The remaining papers of the session were concerned with high-temperature equilibria; C. W. Haworth (University of Oxford) described tungsten-resistor furnaces in which specimens weighing 1–5 gm. can be annealed *in vacuo* or in argon up to 2,700° C. and then quenched. The apparatus has been used in work on molybdenum base alloys. A. Hellawell (University of Oxford) directed attention to the face-centred cubic/body-centred cubic transition found in the metals of the first three transition series, and described apparatus which has been used in the thermal analysis of these phase transitions. The influence of various solute elements upon the transition in manganese and iron was shown to be related to the structures of the elements concerned.

The last paper of the session, by P. Gross, D. L. Levi and G. Wilson (Fulmer Research Institute), discussed methods for determining the thermodynamic activities of alloy constituents at high temperatures. Two methods for measuring vapour or reaction pressures have been used—an effusion method (restricted to systems in which the pressure of any constituent does not exceed about 0·1 mm. mercury) applied to alloys containing iron and aluminium at 1,300° C., and also a capillary vessel method where the reaction pressures are beyond the range of the effusion method.

Mechanical Properties at High Temperatures

In a paper on high-temperature mechanical working of molybdenum, E. W. Ward (Woolwich) discussed the factors affecting the breakdown of the arc-cast structure. The microstructures produced by rolling and extruding at temperatures up to 1,800° C. showed that true hot working had been achieved.

Two papers concerned with the measurement of mechanical properties followed. L. M. T. Hopkins (National Physical Laboratory) described determinations of the creep properties of ceramics and high melting-point metals in air and *in vacuo*, respectively. B. L. Mordike and L. M. Fitzgerald (University of Cambridge) are investigating the properties of the refractory metals tantalum, tungsten, niobium and molybdenum, and the carbides of tantalum, tungsten, niobium, titanium, zirconium, vanadium and boron up to their melting points, which lie in the range 2,500–3,500° C. Apparatus to measure the tensile strength of metals, friction of carbides and hardness determinations of metals and carbides were described.

D. M. Gilbey (Farnborough) presented an extension of the simple theory of the thermal stresses in flat plates, so that variations with temperature and stress of the thermal and elastic properties of the material can be taken into account. The stresses calculated by this method for a manufactured graphite were compared with those obtained from the simple theory using constant 'effective values' of the 'constants'.

The session concluded with a paper by D. T. Livey (Harwell) on the high-temperature stability of oxides and sulphides. The behaviour of the stable refractory oxides *in vacuo*, oxidizing and reducing atmospheres was considered; the refractory sulphides are thermodynamically less stable, in general, than the oxides, although the sulphides of cerium and thorium have been used for reactive metals. Kinetic factors, rather than thermodynamic stability, control the degree of reaction between metals and oxides or sulphides, at least for the more reactive metals.

During the symposium, an exhibition of apparatus, refractories, etc., was held at the University Department of Metallurgy. Exhibits were lent by a number of industrial firms, research establishments, and university departments.

J. W. Martin

INVASIVENESS AND SURFACE PROPERTIES OF CANCER CELLS

An informal symposium on the surface properties of cells and their possible bearing on the invasive movements of cancer cells was held at the Chester Beatty Research Institute on July 4. The chair at the morning session was taken by Prof. A. Haddow and in later sessions by Dr. B. Sylvén (Stockholm) and Prof. G. Klein (Stockholm).

Prof. Haddow pointed out in his introductory remarks that the bearing of the surface properties of cancer cells on their invasiveness has received little attention, apart from the microhistological studies of Dr. Coman and his collaborators in the United States. But interest in the surface properties of cancer cells has developed during the past few years, stimulated largely by Dr. M. Abercrombie's studies of cell movements in tissue culture. It had, therefore, been decided to bring together some of those specialists most directly concerned with this largely unexplored field.

Dr. M. Abercrombie (London) then described the conditions for the invasion of normal cell explants by tumour cells in culture. Whether or not invasion occurs appears to be determined largely by the effect that contact between interacting cells has on their

locomotion. In the cell species so far studied, it is found that sarcoma cells invade explants of normal fibroblasts, whereas populations of normal fibroblasts do not invade each other. Sarcoma cells invade because they treat normal fibroblasts like any other substrate for their locomotion. They adhere to and are guided by oriented structure in any substrate, whether cellular or non-cellular.

To a normal fibroblast other fibroblasts are not simply equivalent to substrates; they are obstacles to locomotion. Contact with them results in an adhesion, immobilizing the small-scale membrane activity in its neighbourhood and stopping the cell from advancing in the direction of the adhesion. This is contact inhibition (Abercrombie and Heaysman, 1954; Abercrombie and Ambrose, 1958). Its nature is unknown, but it is possible to reduce it by changing the composition of the liquid phase of the culture (Curtis, unpublished). The behaviour of fibroblasts towards sarcoma cells appears to be different from the behaviour of sarcoma cells to fibroblasts. There is some inhibition of fibroblast locomotion by sarcoma cells which seems to be effected through a diffusible agent. A small number of experiments have shown that explants of sarcoma cells of different type invade each other.

Is it possible that the loss of contact inhibition and increased activity of the cell membrane is related to the uncontrolled growth of tumours? Prof. M. Swann (Edinburgh) described some interesting observations on the growth of soil amœbæ, which suggest that in this organism growth is affected by contacts. Mr. D. Harrison, working in Edinburgh, had studied the growth of *Hartmanella* in sterile culture. Growth in this case appears to be limited by mutual contact, which is reflected, after an early exponential phase, in the fact that the growth-curve of an amœba culture becomes linear over a considerable range, before it finally flattens out. A variety of experiments have shown that this is not due to environmental conditions, but solely to cell contacts. The linear phase can be abolished by treatment with antisera, when the growth-curve remains exponential for much longer. It seems possible that the contact effect is a direct mechanical inhibition of vacuole intake. Treatment with antiserum presumably prevents close contact and so abolishes the inhibition of growth by contact. Although experimentally difficult to carry out, a similar investigation using mammalian cells would be of great interest.

Various physico-chemical techniques are now being used for a direct study of the nature of the cell surface; they were described by Dr. G. C. Easty (London). He first referred to earlier work on the erythrocyte membrane, which indicates that it is of a lipoprotein nature. A direct examination of the membrane is more difficult with mammalian cells, but it is known that tumour cells carry a net negative electrical surface charge which is almost twice that of the homologous normal cells (Ambrose, James and Lowick). Further information has been obtained by G. C. Easty, D. M. Easty and E. J. Ambrose, who have studied the effect of enzymes upon the adhesiveness of tumour cells to glass surfaces by a new centrifugation technique. The most effective enzymes for breaking contacts between ascites tumour cells and glass have proved to be lipase, phosphatases and elastase. These enzymes are thought to react with lipid, phosphate groups and protein, suggesting that the tumour cell surface is also composed of lipoprotein. The increased negative electrical charge could, therefore, be due to an excess of phosphate groups of phospholipid.

A more general biological approach to the changes in cell populations arising during transformation from normal to tumour tissue was then considered by Prof. and Mrs. G. Klein (Stockholm). They have obtained most interesting evidence for a progressive transformation in sublines derived by selective transplantation from a single tumour (*MCIM* sarcoma). The M_{SS} sublines are solid tumours which do not readily produce ascites cells when transferred to the peritoneum, and only produce metastases very late in the growth of the tumour. The M_{AS} sublines readily form ascites tumours and produce early metastases. These stepwise changes in biological characteristics can be correlated quite well with surface changes, the more anaplastic cell types (M_{AS}) showing a higher electrical charge than the M_{SS} types (Purdom, Klein and Ambrose).

Prof. E. Wolff (France) described a valuable technique using organ culture with mixed tissues and mixed species for the study of invasive movements. Real organ chimeras can be produced from associated duck and mouse testes in which testicular tubules may be formed from cells of the mixed species. In fragments of chick and mouse lung also, the mouse bronchial tubes grow and branch in pure chick connective tissue. Sometimes the two epithelia join and form a common canal. These results indicate that homologous tissues of the two species show more mutual affinities than heterologous tissues of the same species. Several sarcomas have been examined under the same conditions by Prof. Wolff. Fusion between embryo and tumour first occurs. All tumours then show a marked tendency to invade a number of organs, such as mesonephros, metanephros, gonad, skin, intestinal coat, lung, liver, etc. Carcinoma cells show a marked tendency to invade similar tissues to sarcomas, although they retain some capacity to proliferate as dense gatherings or secondary nodules.

Direct histological studies of growing tumours were described by Dr. B. Sylvén (Stockholm). With epithelial tissues in both normal regeneration and tumour growth, the connective tissue exhibits the following changes: (1) a general increase in water content; (2) an increased metachromatic component and (3) appearance of alkaline phosphatase in the ground substance. The extent of the changes gives a measure of the growth-rate and degree of malignancy of the tumour. With normal regeneration, the original connective tissue structure is reversibly restored with cessation of growth. The actual invasion of neighbouring tissues by tumour cells is seen to occur through channels and cavities already present in the normal structures; in addition, a considerable release of enzymes, particularly proteases, occurs. Such a transformation suggests a primary defect in the organization of the malignant cell membrane leading to increased permeability. Incidentally, malignant cells also show an increased permeability to glucose. Such a penetration of enzymes could remove surface adsorbed protein and account for the decreased adhesiveness and high negative charge of tumour cells.

Prof. K. Setälä (Helsinki) then described some experiments which may give a bearing on the actual mechanism of the cellular transformation which gives rise to the altered properties of tumour cells. He described how a number of surface-active agents of the 'Tween' detergent type can act as powerful promoters in carcinogenesis; that is, they lead to a

marked increase in tumour incidence when combined with a given carcinogen. Electron microscopy of the epidermal cells of the interfollicular areas of a mouse's back indicate that marked changes in cell contacts with intercellular gaps and bridges are produced by the promoting agents. Surface-active agents which do not act as promoters, on the other hand, lead to an actual hindrance of proliferation and increased regions of close contact between the cells.

Dr. E. H. Mercer (London) also described some of the valuable results he has obtained by high-resolution electron microscopy of cell contacts. Electron micrographs of cell membranes (Birbeck and Mercer) indicate that they consist of a layer structure about 60 A. thick which could correspond to the lipid lying between protein layers, as proposed by Prof. J. F. Danielli. The membranes are generally separated by a distance of 150–200 A., suggesting the presence of a cementing material between the cells. Anaplastic tumours often show changes in their cell contacts as compared with normal tissues. They may show a convoluted surface with only small areas of contact; the contacts are more like those of normal cells during the early stages of tissue formation. The electron microscopy, therefore, supports the view that the surface properties of tumour cells are changed in comparison with the normal cells from which they are derived.

In conclusion, mention may be made of two other techniques which are being applied to the problem of cell movements and cell contacts. Dr. H. Harris (Oxford) described a simple but most effective method which he has applied to the study of groups of white blood cells. A long exposure is made with dark-field illumination. On subsequent development of the plate, the paths of the moving cells are recorded as streaks on the photographic emulsion. This technique is particularly useful for the study of a taxis affecting the over-all direction of cell migration.

Finally, Dr. R. J. Goldacre (London) described an approach based on the use of electronic models. In normal growth and maintenance the transfer of information from cell to cell evidently occurs. Direct contacts between the cell membranes appear to play a part in this, at least in the early stages of development. An electronic model consisting of units ('cells') which can stimulate and be stimulated by others can be designed. By connecting the units together in different groups, various complex patterns of interest in morphogenesis are generated in the system; for example, patterns with polarity, discrete differences between neighbouring units, etc. On the basis of such a picture, it would be expected that a small loss of cell – cell interaction, arising from surface changes, could readily lead to abnormal and uncontrolled growth in tumour tissues.

E. J. AMBROSE

PREDICTING ACADEMIC SUCCESS

THE purpose of a recent investigation by Sigvard Rubenowitz, of the Swedish Council for Personnel Administration, Gothenburg, was to determine the weights which have to be assigned to different tests and biographical data in order to predict success in academic studies*. The freshmen at the three universities in Gothenburg in 1954 were invited to take part in the investigation, the results of which would later be related to success at university as measured by examination results. Freshmen were chosen as subjects for the investigation in order to avoid bias in the results of the tests arising from different academic studies. In all, 440, or 62 per cent, of the freshmen responded to the invitation.

After two years, information about examination results was collected and this was related to the data collected two years earlier.

The data collected and the tests which were given to the students were: (1) grades in the matriculation examination; (2) study habit assessments; (3) intelligence test marks; (4) technical test marks; (5) mathematical–technical test marks; (6) organization test marks; (7) details of interests; (8) psychodiagnostic test assessment; and (9) attitude assessment.

Analysis of the results showed that of 43 female students who studied languages and 18 who were studying psychology the validation data in Table 1 were obtained.

It became clear that, for languages, more time is required for study than for other subjects. In addition, a significant correlation exists between intellectual and matriculation results on one hand and success in language studies on the other. The study habit also appears to be of great importance in the study of languages. With psychology, general intelligence, together with those qualities which find expression in a good matriculation result, are not of such decisive importance as are certain mathematical technical aptitudes and some characterological factors that are measured by the Zulliger test.

Table 1

	Languages, 43 students	Psychology, 18 students
Grades in matriculation examination	0·43	0·12
Study habit inventory	0·38	0·17
Intelligence test	0·40	0·28
Technical test	0·17	0·31
Mathematical–technical test	0·06	0·23
Organization test	0·04	0·28
Psychodiagnostic test	0·15	0·37
Attitude assessment (the 'rigid' pole)	0·21	0·25

With certain male students the subject groups that formed the object of the validation were languages, psychology (philosophy), mathematics (statistics) and zoology (botany). The students of mathematics and statistics were, in general, superior to all others and above all in their intelligence and mathematical–technical ability. The male language students, like their female counterparts, made a significantly poor showing in their examination results.

The validation data in Table 2 were obtained from this inquiry.

Comparing these results with those for female students, the same trend is found except in the case of the matriculation result; this was of most value in prognosis for female students of languages, whereas for male students its value is highest for prognosis of psychological studies.

* *Occupational Psychology*, **32**, No. 3 (July 1958).

Table 2

	Languages, 35 students	Psychology, 15 students	Mathematics, 12 students	Zoology, 10 students
Grades in matriculation examination	0·09	0·53	0·58	0·08
Study habit inventory	0·25	0·14	0·50	0·42
Intelligence test	0·33	0·31	0·32	0·29
Technical test	0·18	0·43	0·47	0·25
Mathematical–technical test	0·22	0·25	0·61	0·06
Organization test	0·34	0·11	−0·04	0·01
Interest blank. (University Arts Faculties Scoring Scheme)	0·06	−0·65	−0·37	−0 30
Interest assessment (Chalmers University Scoring Scheme)		0·49	0·42	
Psychodiagnostic test	0·55	0·62	0·38	0·49
Attitude formula (the 'rigid' pole)	0·17	0·13	−0·08	0·03

At the University of Technology the coefficients of validity in Table 3 were obtained.

It appears that the matriculation examination has a considerably higher prognostic value for these than for those at the University (arts faculties), probably because the courses at the former have to be followed closely and in many respects resemble pre-matriculation studies. For this reason, the matriculation examination can be considered as a job sample test.

A combination of the matriculation results and tests would form the most suitable instrument of prognosis for these students, provided that the multiple regression calculation stands up to cross-validation in a renewed investigation.

Table 3

	219 students
Grades in matriculation examination	0·67
Study habit inventory	0·30
Intelligence test	0·15
Technical test	0·22
Mathematical–technical test	0·32
Organization test	0·09
Interest blank	0·20
Psychodiagnostic test	0·22
Attitude assessment (the 'rigid' pole)	0·01
Entrance qualifications (matriculation grades + previous factory experience)	0·52
Best combination of six prognostic variables	0·77

At the University of Economics the criterion used was the average result in all the subjects passed. The coefficients of validity were as shown in Table 4.

Table 4

	49 students
Grades in matriculation examination	0·22
Study habit inventory	0·46
Intelligence test	0·18
Technical test	0·31
Mathematical–technical test	0·34
Organization test	0·18
Interest blank	0·16
Psychodiagnostic test	0·36
Attitude assessment	−0·04
Best combination of seven prognostic variables	0·77

The study habit inventory had the highest validity here, followed by Zulliger's psychodiagnostic test and the mathematical–technical test. The low validity of the matriculation result is worthy of note.

INDUSTRY AND GOVERNMENT IN CANADA

IN his Messel Lecture, "Industry and Government in Canada", before the Society of Chemical Industry at Montreal on September 15, the Rt. Hon. C. D. Howe, P.C., reviews changes in the responsibilities of government and the attitude of industry during the past fifty years. When he came to Canada as a graduate engineer in 1908, Mr. Howe said that most people regarded activities at Ottawa as remote and of very little personal concern. Now, an industrial revolution and relatively sudden highly scientific industrial and military developments, with the rise of the Welfare State, had transformed the scale and character of government administrative responsibility. While the population had grown from 6·5 million to 17 million, government expenditure had multiplied about twenty-five times and was now 5,272 million dollars a year. Mr. Howe believed that most Canadian business men to-day recognized that the public demanded services which only government could provide and that many of them not only tolerated government activity but also were prepared to admit that government action could promote the prosperity and welfare of the country. There had also been a similar improvement in the attitude of government towards business in Canada, and his experience as a Minister during 1935–57 led him to believe that the role of industry and commerce in society was better understood than it had been before.

Mr. Howe then referred to some changes in the administrative structure and notably the appearance of what is known in Canada as the Crown Corporation, on which experienced business men gave part-time service as directors. This pragmatic device, analogous to the public corporation in Britain, had received much more extensive use since 1935, and after noting the establishment of the National Research Council as a Crown Corporation, out of the Advisory Council on Scientific and Industrial Research formed in 1916, Mr. Howe described a few examples including some of the twenty-eight Crown Corporations formed during the Second World War in the Department of Munitions and Supply, of which he became Minister in 1940. During and after the War the Department functioned directly as the sole procurement agency for the three Armed Services, and he thought that the Crown Corporation had proved itself to be an efficient device for enabling government to cope with certain new responsibilities thrust upon it by an advancing technology. Generally, he thought that the government should not enter into any business that is competitive with private industry, but certain responsibilities that could not be directed to private industry and certain other responsibilities which no private industry was prepared to undertake were most efficiently discharged through a Crown Corporation, nor did he think the device need be abandoned if private industry later entered the field. He also thought that the Crown Corporations had made an important contribution to better understanding between government and business, and in his twenty-two years experience it had been amply demonstrated that complete co-operation between government and business is a prerequisite of national prosperity.

A NATIONAL TYPE CULTURE COLLECTION OF MARINE BACTERIA

By Dr. J. M. SHEWAN, G. D. FLOODGATE and P. R. HAYES

Torry Research Station, Aberdeen (Food Investigation Organization, Department of Scientific and Industrial Research)

FOR many years now, work has been proceeding at the Torry Research Station on the bacteriology of marine fish and on the changes in flora occurring during spoilage and processing. It has generally been recognized that the identification of most of the organisms concerned is one of extreme difficulty. It has often been impossible to be sure of the correct family or tribe, let alone the species. These difficulties are not, of course, confined to the microflora of fish; they are also encountered through the whole of marine bacteriology and especially in the *Achromobacter*, *Pseudomonas* and *Vibrio* groups.

A primary handicap has been the disappearance of the type species of many of the genera commonly occurring in marine, soil, air or fresh water environments. Thus, so far as we are aware, authentic cultures of *Achromobacter liquefaciens* and *Flavobacterium aquitale*—the type species of these two genera in Bergey's determinative manual[1]—no longer exist in any type culture collection. Moreover, the descriptions of these organisms in the literature as well as those of many related species are completely inadequate. One example of the confusion that has arisen may be mentioned. Wells and ZoBell[2] in 1932 isolated an organism from the skin lesions in the California killifish and named it *Achromobacter ichthyodermis*. In the original description no mention was made of several features now regarded as essential for taxonomic purposes, for example, type of flagellation and mode of dissimilation of glucose, so that the organism could well be placed in either the *Achromobacter*, *Pseudomonas*, *Aeromonas* or *Vibrio* genera. Indeed, it is classified as a *Pseudomonas* in the 1957 edition of Bergey's manual and as *Achromobacter* by Brisou[3]. In 1950, an organism was isolated at this Station from a lesion in plaice and provisionally classified as a *Pseudomonas* sp., and within the past two years Baage and Baage[4] have isolated a bacterium from lesions in Baltic cod which they believed to be identical with *Vibrio anguillarum*[5], the causative organism of the classical 'red disease' of eels. Recent comparison here of these three organisms has shown that they are closely allied, if not identical, and are probably vibrios. Unfortunately, no authentic culture of *Vibrio anguillarum* appears to be available in any type culture collection, so that the complete identity of these three isolates with *Vibrio anguillarum* must remain in doubt.

It is not surprising, therefore, that investigators frequently state that the bacteria that they have isolated do not fit any description given in Bergey's manual or any other determinative system. Consequently, a multiplicity of species, nomenclatures and taxonomic groupings has arisen. We have recently examined more than 100 cultures, 70 from Scandinavia and 30 from North America and all from marine sources. In only about 30 instances did our taxonomic positioning agree with that of the senders, simply because of the divergence of opinions as to which characters are of taxonomic significance.

It is, of course, recognized that a chief difficulty in classifying bacteria from air, soil and water is that the available diagnostic tests, which arose mainly from the detailed studies of animal and human pathogens, yield almost invariably negative results. It is clear that a much more detailed study of the non-pathogens is required and in particular of the Gram-negative asporogenous rods—the *Achromobacter*, *Pseudomonas*, *Flavobacterium* and *Vibrio* groups—to reduce the present chaos to order. New tests of taxonomic significance will have to be found and will only be forthcoming from a thorough study of the biology, physiology and biochemistry of these groups in question.

To begin such a study two essentials at least are required.

(1) The re-isolation and full description of the type species mentioned above, or, where this is impossible, an agreement among taxonomists that a particular organism, known to exist, shall in future be designated the type culture.

(2) The setting up of type culture collections so that cultures are available for comparative purposes: frequently, papers are published that describe apparently new species, none of which has been kept viable or been deposited in a type culture collection.

There appear to be few type culture collections of marine bacteria anywhere outside of the United States. Prof. C. E. ZoBell at the Scripps Institute, La Jolla, California, and Prof. C. E. van Niel at the Hopkins Marine Station, Pacific Grove, California, both maintain small but valuable collections. A few marine strains are held in private collections and at the Pasteur Institute, Paris, and the Microbiological Institute, Delft, and, no doubt, elsewhere. For years the Torry Research Station has maintained a small collection of bacteria mainly from marine fish and solar salts. The need, however, of putting this collection on a more permanent basis and of more detailed studies of the various groups, with the view of better taxonomy, has now been recognized. Marine bacteria play an important part not only in fish spoilage but also in the deterioration of submerged materials, nets, seaweeds, as well as in the biological cycles in the sea. As a result of consultations between various Government Departments, the Development Commission and the University of Aberdeen, funds and personnel have been made available for broadening the basis of the collection held at Torry so as to include bacteria from all marine sources and for a start to be made on more detailed studies of certain selected groups. The present collection, which will form one of the British national collection of type cultures, comprises some 200 named strains of marine bacteria in addition to several hundred recently isolated unnamed strains. All these organisms are at

present maintained on culture media and work is now proceeding to test the best method for their long-term preservation.

The collection, though small, is already becoming known to many research workers. Last year more than 100 cultures were sent to laboratories all over the world, but it will take some time to develop it and to prepare a catalogue.

Meantime, bacteriologists are invited to deposit cultures of marine bacteria in the collection, particularly so that their isolates may not be lost but be made available for future comparison. In this way it is hoped that some measure of progress may be made in establishing, on more solid foundations than hitherto, the taxonomy of marine bacteria.

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SOME NEW NEUROMUSCULAR BLOCKING AGENTS

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FOR muscular relaxation in anæsthesia, suxamethonium has the advantage of brevity of action but the disadvantage of possessing no satisfactory antagonist and of sometimes causing post-operative muscle pains and stiffness[1]. Laudexium (laudolissin)[2] is antagonized by neostigmine and does not, so far as we know, cause muscle pains, but it is of longer duration of action than suxamethonium. It occurred to us that it might be possible to prepare an agent combining the valuable properties of both compounds by incorporating some of the chemical features of each into one molecule.

Three series of compounds were investigated. *Type I : Symmetrical bis-esters.* These were prepared by (*a*) the quaternization of N-alkyltetrahydropapaverines with a suitable ω-bromoalkyl ester or (*b*) the reaction of tetrahydropapaverine with an ω-bromoalkyl ester, and quaternization of the resulting bis-tertiary amine with an alkyl halide or sulphate. *Type II : Unsymmetrical mono-esters*, which were obtained from the dialkylaminoalkyl esters of ω-bromo-aliphatic carboxylic acids by quaternization with an alkyl halide, and subsequent treatment of the product with an N-alkyltetrahydropapaverine. *Type III : Symmetrical bis-amides.* The reaction of dicarboxylic acid chlorides with excess ethyleneimine yielded bis-amides of structure :

$$Cl—(CH_2)_2—NH—CO—(CH_2)_n—CO—NH—(CH_2)_2Cl$$

which, after conversion to the corresponding di-iododerivatives, were then quaternized with N-alkyltetrahydropapaverines to yield the required products. The use of phosgene instead of a dicarboxylic acid chloride resulted in the corresponding urea derivatives (IV).

All compounds were examined by intravenous administration to cats, maintained by artificial ventilation and prepared for recording arterial blood pressure and the isometric twitch of the tibialis anterior muscle in response to stimulation of its motor nerve, as described by Paton and Zaimis[3]. The potencies and durations of the neuromuscular blocking actions of the new compounds were compared with those of suxamethonium chloride, or occasionally of (+)-tubocurarine chloride or laudexium methosulphate. Neostigmine methosulphate was given in antagonism tests on some of the new compounds studied. All doses are expressed as weights of salts.

In order to establish norms of potency and duration all doses of the three reference compounds that caused more than 74 and less than 100 per cent depression of the tibialis twitch in all experiments between June 1951 and June 1956 were pooled to obtain overall mean values. These showed that the ratio of potencies in the cat of suxamethonium : (+)-tubocurarine : laudexium was 1·0 : 0·16 : 0·28, and the corresponding ratio of durations was 1·0 : 4·6 : 4·0. Laudexium did not differ significantly from (+)-tubo-

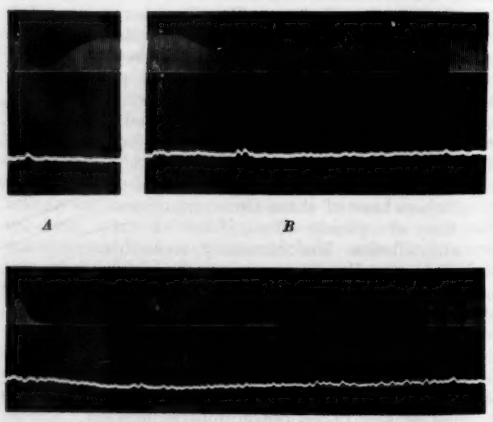

Fig. 1. Effects of suxamethonium and compound 43 on neuromuscular conduction and blood pressure in the cat. Upper tracing, tibialis twitch in response to stimuli to motor nerve, repeated at 6/min.; lower tracing, carotid blood pressure; dot indicates time of dosage. *A*, 60 μgm./kgm. suxamethonium chloride; *B*, 7, and *C*, 10 μgm./kgm. compound 43 bromiodide

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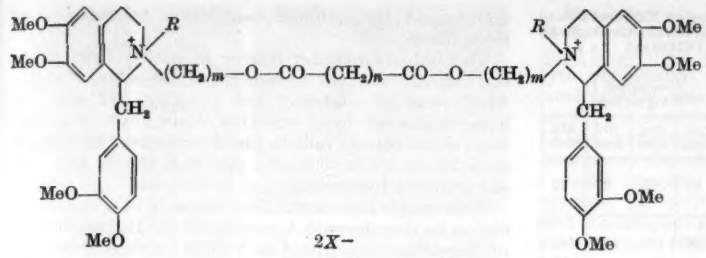
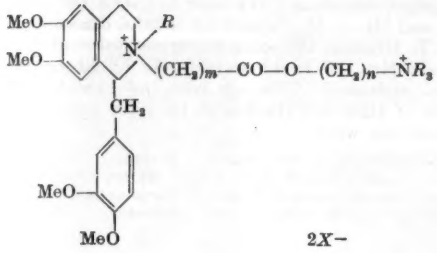


(I)



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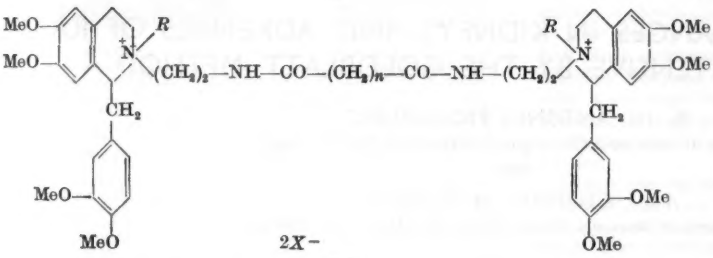

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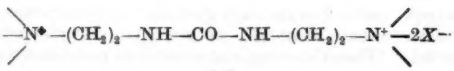

(IV)

(—N⁺ = N-alkyltetrahydropapaverinium)

curarine in duration, although, in an initial more limited series of experiments published previously, it appeared to be longer in duration[4].

The results obtained in the cat with the new compounds described above are illustrated in Fig. 1 and summarized in Table 1, from which it will be seen that the only compound more potent than suxamethonium was the unsymmetrical mono-ester, No. 43, and the only compound briefer than suxamethonium was the symmetrical *bis*-ester, No. 41.

Compound 43 was about seven times as active as suxamethonium. It was of long duration of action and did not show antagonism by neostigmine. It was given to one cat at a dose of 500 μgm./kgm. (that is, about 50 times a fully effective dose). Blood pressure fell to about 82 per cent and then rose to about 150 per cent of its value before treatment; the cat survived for 1 hr., and was then destroyed.

Compound 41, although relatively weak, was antagonized by neostigmine in the cat. The cumulative actions of suxamethonium and compound 41 were compared in three cats, in which series of successive equal doses of one substance were given at equal intervals of time. In these experiments, later doses of compound 41 did not last longer in effect than the initial dose, but later doses of suxamethonium were both more long-acting and more effective than the earlier. Table 2 illustrates this finding in one such experiment.

One cat received 20 mgm./kgm. compound 41, which was about six times a fully effective dose. This caused a complete neuromuscular block lasting 34 min. to 75 per cent recovery. There was a 43 per cent fall in blood pressure. At 2¾ hr. after this dose, the cat was alive; a dose of 40 mgm./kgm. then caused a further fall in blood pressure and the cat died.

In conclusion, a search for neuromuscular blocking agents resembling (+)-tubocurarine in mode of action, but briefer in duration, resulted in the

Table 1. Summary of Results obtained with Compounds in Cats. Blood Pressure Observations made at Fully Effective Doses

Compound						No. of cats	Approximate relation to suxamethonium (= 1)		Fall in blood pressure	Neostigmine antagonism
Type	No.	*R*	*m*	*n*	2*X*		Potency	Duration		
Bis-ester (I)	31	CH_3	2	2	2Br	3	0·06	5·4	×	+
	32	CH_3	2	1	2Br	8	0·15	2·6	+	+
	35	CH_3	2	4	2Br	2	< 0·01	—	+	−
	36	C_2H_5	2	1	2Br	2	< 0·01	—	−	−
	38	CH_3	3	1	2Br	3	0·3	9	×	+
	39	CH_3	2	0	2Br	3	0·002	—	+	−
	41	CH_3	3	0	2Br	8	0·025	0·5	×	+
Mono-ester (II)	43	CH_3	5	2	BrI	4	7·0	6·3	×	×
	47	CH_3	4	3	BrI	3	< 0·5 > 0·05	8	×	−
Bis-amide (III)	45	CH_3	0	0	2I	2	0·02	2·5	×	+
Bis-amide (IV)	44	CH_3	0	0	2I	2	0·01	1·5	×	+

× = No effect; + = some effect; − = not tried

Table 2. Cat Tibialis. Extent and Duration of Neuromuscular Depression caused by Suxamethonium and Compound 41, given in Doses repeated at 20-min. intervals

Effect	Suxamethonium, 50 μgm./kgm.				Compound 41, 3 mgm./kgm.			
	1st dose	2nd dose	3rd dose	4th dose	1st dose	2nd dose	3rd dose	4th dose
Depression tibialis t witch (per cent)	69	83	88	94	69	65	74	75
Duration to 75 per cent recovery (sec.)	190	290	370	340	130	120	150	140

synthesis of three series of bis-quaternary ammonium salts, all possessing structural features in common with laudexium and suxamethonium.

The only compound more active than suxamethonium in the cat was the unsymmetrical mono-ester, No. 43, which was about seven times as active as the reference compound and appears to be one of the most powerful synthetic neuromuscular blocking agents known. It was of long duration of action and did not show antagonism by neostigmine. Cats maintained by artificial ventilation tolerated very large doses.

The only compound briefer in action than suxamethonium was the symmetrical bis-ester, No. 41, which was of relatively low potency. It was not hypotensive at fully effective doses, but relatively large doses caused falls in blood pressure. It was not cumulative when given in repeated doses, and was antagonized by neostigmine in the cat.

This article represents the substance of a communication to the eleventh Congress of the Italian Society of Anæsthesiology, held in Venice on September 12–15. Full chemical and pharmacological details will be published elsewhere. We wish to thank Dr. J. G. Bourne and Mr. G. M. Timmis for helpful discussions, Mr. R. T. Brittain for some experimental contributions, and Mrs. E. Nield and Mr. I. J. Gibson for technical assistance. We are also indebted to the Directors of Allen and Hanburys, Ltd., for permission to publish this work.

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HISTOCHEMICAL CHANGES IN KIDNEYS AND ADRENALS OF RATS MADE HYPERTENSIVE BY THE GOLDBLATT METHOD

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GOLDBLATT and his colleagues[1] showed that partial constriction of the renal artery and removal of the opposite kidney induces persistent hypertension. In the dog and rabbit, hypertension is transient unless the opposite kidney is removed, but in the rat[2,3] persistent hypertension occurs after constriction of one renal artery without contralateral nephrectomy. In such animals hypertensive vascular lesions, similar to those found in malignant hypertension in man, develop in the opposite or 'untouched' kidney but are never found in the kidney with renal artery constriction (the 'clipped' kidney). Floyer[4,5] demonstrated that in rats with hypertension of several weeks duration, produced by renal artery constriction and before vascular lesions had developed in the contra-lateral kidney, removal of the clipped kidney restored the blood pressure to normal in a few hours, but the removal of both kidneys had no effects. Since denervation experiments have no effect upon this experiment, Floyer[4,5] suggested that the clipped kidney secreted a substance (renin ?) which altered the blood pressure regulating function of the untouched contra-lateral kidney. Since adrenalectomy abolishes hypertension the adrenals presumably are part of the pressor mechanism which comes into operation when the kidney is rendered abnormal by clipping.

A variety of histochemical techniques were applied to both kidneys and adrenals of rats on which partial renal artery constriction had been carried out by the method of Wilson and Byrom[2]. Some animals were subjected to exactly the same procedure as above but using larger clips which simply hung as a loose collar around the artery and did not compress it at all—this did not give rise to hypertension but caused some decrease of succinic dehydrogenase reaction. The following histochemical reactions were studied at varying times following these two types of ligation (clipping): succinic dehydrogenase, acid and alkaline phosphatase, 5-nucleotidase, simple esterase, lipid, cholesterol and periodic acid Schiff-positive sub-

Table 1

	Acute animals	Chronic animals
Succinic dehydrogenase	In clipped kidney decrease within 2 days, persisting to 8 days	Clipped kidney normal. Contra-lateral kidney almost normal but negative in patches
Phosphatases Alkaline phosphatase Acid phosphatase 5-Nucleotidase	Reduction of all three phosphatases, greatest in clipped kidneys. Alkaline phosphatase normal by 8 days. 5-Nucleotidase normal by 18 days. Acid phosphatase still decreased at 18 days	All three phosphatases decreased in contra-lateral kidneys. Almost normal in clipped kidneys
Simple esterase	Increased in both kidneys	Decreased in both kidneys
Lipids and cholesterol	Accumulation of lipid in glomeruli of both kidneys at 2 hr. Later accumulation in groups of tubules most obvious in contra-lateral kidney. No cholesterol demonstrated	Tubular lipid only in clipped kidneys. Contra-lateral kidney shows lipid and cholesterol in glomeruli

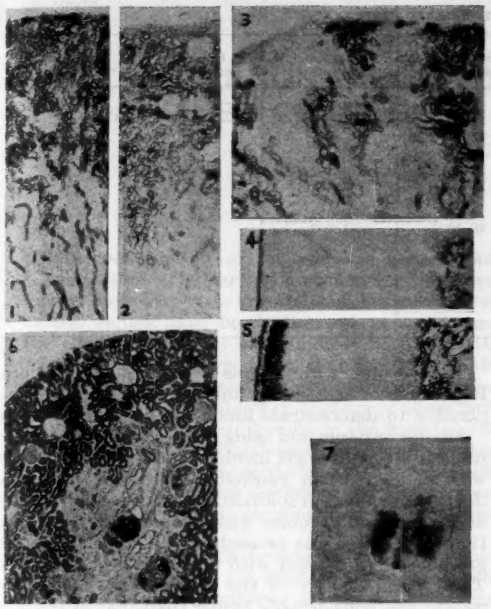

Fig. 1. Succinic dehydrogenase reaction in normal rat kidney. 2, Succinic dehydrogenase reaction in rat kidney (clipped side) with partial clipping of renal artery for five days. Greatly reduced reaction. 3, Succinic dehydrogenase reaction in contra-lateral kidney of rat with renal artery of opposite kidney partly clipped for two months. Reaction almost negative in parts, normal in some patches. 4, 5-Nucleotidase in adrenal of normal rat. Reaction is restricted to the capsule, the narrow zona glomerulosa and the medulla. 5, 5-Nucleotidase in adrenal of rat with one kidney partly clipped for two months. Great increase in zona glomerulosa and in 5-nucleotidase reaction in glomerulosa and medulla. 6, Sudan black (lipid) preparation of contra-lateral kidney of rat with renal artery of opposite kidney partly clipped for two months. Note accumulation of lipid in tubules and in glomeruli. 7, Same animal as in Fig. 6. Schultz cholesterol preparation. A single glomerulus showing accumulation of cholesterol

stances. 'Acute' animals in this account means those animals which have been clipped for periods up to a few weeks and showed no hypertension. 'Chronic' refers to those animals which had been clipped for some months and had developed hypertension. The results are shown in Table 1.

In all animals from 2 days on there was an increase in the width of the zona glomerulosa of the adrenals (said to produce the hormones responsible for electrolyte regulation) accompanied by an increased 5-nucleotidase reaction. There was a decrease of alkaline and acid phosphatase in the cortical sinusoids in the acute animals, and an increase of acid phosphatase in the chronic animals.

Light clipping of one renal artery thus produces changes in activity and distribution of enzymes and accumulation of lipid in both kidneys within two hours. More profound changes occur in both kidneys and adrenals within two days. Within three weeks most, but not all, of these changes have returned to normal in the clipped kidneys. In the contra-lateral kidneys some changes persist into the chronic stage and presumably play a part in the development of pathological changes there. The changes in the adrenals persisted or increased in chronic (hypertensive) animals. Attention should be directed to the accumulation of cholesterol in the glomeruli of the contra-lateral kidney in chronic animals, to the fact that the histochemical changes occur very quickly and precede both pathological changes and hypertension and to the fact that even placing a clip in position around the renal artery without any compression at all causes changes in the succinic dehydrogenase activity of the clipped kidney.

The cause of these changes is not yet established; but their existence must lead to speculation as to whether the renal artery itself, in response to irritation, is not capable of secreting a substance which, by affecting the clipped kidney, causes the whole cycle of events which lead to the initiation of hypertension.

This work was assisted by a grant from the Medical Research Council to Dr. A. Pasqualino. We are greatly indebted to Dr. M. A. Floyer of the Medical Unit, The London Hospital, Whitechapel, for the provision of clipped rats for this work and for much helpful comment and details of literature.

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MELANIN: A NATURALLY OCCURRING CATION EXCHANGE MATERIAL

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IT is the purpose of this report to present results which demonstrate that melanin from two different sources has strong cation exchange activity.

Although melanin is a substance of immense sociological and physiological significance, little is known of its structure, reactivity, physical state, or of the functions which it may possess. Greenstein[1], Mason[2] and others[3] have characterized the elementary composition, some precursors and certain physical facts about some plant and animal melanins. Commoner *et al.*[4] have shown that melanin contains stable free radicals, and have commented on the chemical significance of this fact.

It has become generally accepted that melanins are complex polymeric substances intimately bound to protein. *In vivo*, melanin is thought to exist as particles of 0·1–1·0μ diameter. Crude preparations of melanin granules are completely insoluble in water and all common organic solvents; the granules are soluble in hot aqueous sodium hydroxide, in which melanin probably undergoes depolymerization; melanin is apparently soluble in dilute sodium carbonate[1]. Dried preparations of granules take up 2–4 times their weight in water. These physical characteristics: complex polymeric structure (thought to be derived from phenolic precursors), insoluble particulate state,

Table 1. 8·13 gm. of Dry Melanin Particles

Supernatant	Volume ml.	pH	Sodium m.equiv./l.	Sodium m.equiv.	Chloride m.equiv./l.	Chloride m.equiv.
Water wash 1	20·0	6·87	7·30	0·146		
Water wash 2	20·0	6·91	17·83	0·357		
Water wash 3	20·0	7·04	13·95	0·279		
NaCl solution	20·0	6·52	79·60	1·590	81·1	1·620
NaCl supernatant	17·4	6·67	47·80	0·813		
Water wash 4	15·5	7·43	23·85	0·312		
Water wash 5	17·0	7·50	15·00	0·255		
Water wash 6	17·5	7·58	9·45	0·165		
HCl 0·1 *N*	20·0		0·50	0 010		
HCl supernatant	27·3	2·20	40·40	1·090		
NaOH supernatant	16·8	7·94			60·5	1·011
NaCl supernatant	20·0	7·50			69·1	1·382
Water wash 7	18·0	7·40			34·1	0·614
Water wash 8	18·5	7·12			28·2	0·521
Water wash 9	17·5				9·6	0·168
NaOH 0·1 *N* supernatant	13·0				8·6	0·119

and the ability to take up large amounts of water are strongly reminiscent of some of the chief characteristics of synthetic organic ion exchange resins[5]. Therefore, the ion exchange activity of partially purified melanin was examined.

The sources of the melanin used in the following experiments were the transplantable Harding–Passey tumour of mice, taken after eight weeks of growth in *C57/dba* hybrids, and the ink from the ink sac of the Pacific coast squid (*Loligo opalescens*). The tumour (657 gm.) was homogenized in dilute sodium chloride solution and the granules separated by high-speed centrifugation, as described by duBuy *et al.*[6]. The granules obtained were uniform in colour, size and shape. From the starting weight of tumour, 28 gm. of wet melanin granules were obtained. On drying over calcium chloride *in vacuo* a final yield of 13·0 gm. of coal-black lumps was obtained. Squid ink granules were obtained by repeated washing of the particles with water, and high-speed centrifugal separation. The very small particle size of both preparations prevented the use of columns or conventional filters. The washed granules were incubated with dilute saline, washed further and then treated with 0·1 *N* hydrochloric acid. Further centrifugation gave the hydrochloric acid supernatant. All these centrifugal supernatants were collected separately, the *p*H was measured, and the sodium ion content measured. The *p*H of the granules treated with hydrochloric acid was then adjusted to 7·9, the granules washed, treated again with sodium chloride, washed further, and then incubated with hydroxyl, formate or acetate. The *p*H and chloride ion content of each supernatant were measured.

A similar study was performed with aqueous eosin, in which granules were incubated with the eosin solution at neutral *p*H, then washed until the supernatant was free of eosin, treated with 0·1 *N* hydrochloric acid, and the eosin content of the hydrochloric acid supernatant measured.

Table 1 gives a résumé of results in a typical experiment. Incubation of washed melanin granules with sodium chloride appeared to decrease the sodium ion content of the supernatant fluid. Most of this 'lost' sodium ion content reappeared on further washing of the granules, and probably had been retained in the interstices of the granules. Hydrochloric acid, however, eluted a very considerable amount of sodium ion from the melanin with a marked drop in *p*H. It should be emphasized that the amount of sodium ion content found in the supernatant may represent only about half of that actually eluted, for approximately 20 ml. of fluid remained with the granules after each centrifugation.

The results with anions were equally uniform. Regardless of the eluting anion employed, it was not possible to demonstrate anion elution from melanin.

Similar experiments using eosin gave corroboratory results. At neutral *p*H incubation of melanin granules with aqueous eosin markedly decreased the optical density of the eosin solution. After repeated washing of the melanin granules with water, until no absorption at 515 mμ was present in the supernatant, the granules were treated with 0·1 *N* hydrochloric acid. The optical density of the hydrochloric acid supernatant was considerably higher than that of the wash solutions, despite further dilution of eosin. (Treatment with hydrochloric acid of melanin particles not incubated with eosin did not produce any material in the supernatant absorbing at 515 mμ.)

The cation exchange activity of squid melanin was similar to that of mammalian melanin. Squid melanin particles appeared to have a higher level of cation-exchange activity than did the mammalian particles; but this may be due to the greater contamination of the latter.

The results of these experiments indicate that melanin granules from both a mammalian and an invertebrate source have the capacity to act as cation-exchange materials of considerable activity. Bersin[7], who has discussed naturally occurring cation exchangers in man, includes tyrosinase, ceruloplasmin, ascorbic acid oxidase and transferrin. To this short list melanin can be added.

The significance of this cation-exchange activity of melanin in relation to function is speculative, but of great interest. Cassidy[8] has shown that some cation exchange polymers can also absorb electrons. The distribution of melanin in normal animals in areas exposed to light, and its increase in the skin after exposure to sunlight or ionizing radiation make for interesting speculations as to the importance of the ion-exchange activity of melanin as one of its more important functions.

This work was supported by a grant (*CY* 2914) from the National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

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INCORPORATION OF CARBON-14 DIOXIDE INTO SUGARS BY DARKENED COTYLEDONS FROM ETIOLATED SUNFLOWER SEEDLINGS

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THE consumption of fat and the concomitant production of sugars by germinating sunflower seedlings have long been known, and low respiratory quotient values have been observed to accompany these changes. Recent experiments[1] with etiolated sunflower seedlings have shown that the acids of the tricarboxylic acid cycle also accumulate during germination. One possible explanation of these facts is that fixation of carbon dioxide in the β-carboxylation of pyruvate or phosphoenol pyruvate to yield oxalacetate or malate contributes to this accumulation, as happens when low respiratory quotient values accompany malic acid accumulation in darkened *Kalanchoë* leaves.

Accordingly, carbon-14 dioxide was fed to darkened cotyledons (usually 2–6 gm. fresh weight), which were cut from 5-day-old sunflower seedlings which had been grown in the dark at 20° C. The darkened vessels containing the tissue were flushed with air free from carbon dioxide for 1 hr. before the introduction of the carbon-14 dioxide. After exposure to carbon-14 dioxide (about 0·5 mc.) for periods of 5 sec.–12 hr., the cotyledons were exhaustively extracted with 80 per cent ethanol. Components in this extract were identified by two-dimensional chromatography on Whatman No. 1 paper with *tert.* amyl alcohol/formic acid/water and propanol/ammonia as developing solvents. Amino-acids were also chromatographed separately after fractionation of the ethanolic extract on ion-exchange resins. Radioactive components were detected by radioautography and the carbon-14 content of individual substances was assayed by counting the active areas on the developed chromatograms. Since all experiments were performed on seedlings of the same age, it has been assumed that all these seedlings contained their various constituents in closely similar proportions, and that the comparison of the relative amounts of radioactivity in the individual substances after varying periods of exposure to carbon-14 dioxide is valid. The malic acid and the glucose moiety of sucrose were degraded by procedures based on fermentation by *Lactobacillus arabinosus* and *Leuconostoc mesenteroides*, respectively.

The most striking result shown in Table 1 is that in experimental periods longer than 5 min. sucrose was the most heavily labelled compound. In earlier work on other tissues fed with carbon-14 dioxide in the dark the free sugars were either unlabelled or possessed only weak activity[2–4]. Even in *Kalanchoë*, which possess exceptionally high powers of dark fixation of carbon dioxide, no labelled sugars have been detected[5].

With shorter periods of carbon-14 feeding, the bulk of the radioactivity was in malate and in related acids and amino-acids, suggesting that carbon-14 dioxide was incorporated by a β-carboxylation of pyruvate or phosphoenol pyruvate to give malate either directly or indirectly by way of oxalacetate. The enzyme system catalysing this incorporation is as yet unidentified, though Walker (private communication) has detected malic enzyme in the cotyledons of 5-day-old sunflower seedlings.

Table 1. Distribution of Carbon-14 among Compounds extracted with 80 per cent Ethanol from Sunflower Cotyledons which had been exposed to Carbon-14 Dioxide in the dark

Substance	Period of dark carbon-14 dioxide fixation			
	5 sec.	45 sec.	5 min.	30 min.
Sucrose	0·0	3·6	294·8	2,242·3
Glucose	0·0	trace	20·5	81·0
Fructose	0·0	trace	19·5	109·8
Malate	48·0	412·3	132·5	242·7
Citrate	0·0	22·1	54·0	105·2
Succinate	trace	31·3	10 0	13·0
Fumarate	1·3	44·5	2·8	5·5
Aspartate	8·5	11·2	41·4	71·9
Glutamate		2·5	1·4	6·0
Alanine	4·5	58·1	26·1	30·8
Serine		0·7	2·4	8·4
Glycine		0·9		
	62·3	587·2	605·4	2,916·6

The results are expressed as c.p.m. × 10^{-3}.

Table 2 shows the distribution of carbon-14 within malic acid and the glucose moiety of sucrose isolated from the cotyledons which had been exposed to carbon-14 dioxide for 15 min. in the dark. In the malate the isotope was essentially confined to the carbon atoms of the carboxylic groups, and it is noteworthy that the carbon-14, presumably first incorporated into the β-COOH group, was after 15 min. rapidly appearing in the α-COOH group. The radioactivity in the hexose was largely confined to the central carbon atoms, that is, carbon atoms 3 and 4.

The identification of malate as an early product of carbon-14 dioxide incorporation and the subsequent accumulation of label in sucrose suggest that malate is converted into sucrose. This conversion could occur by way of the reactions of glycolysis in reverse, with malate giving rise to either pyruvate directly or phosphoenol pyruvate via oxalacetate as the first reactions. In either case, the carbon-14 present in the β-COOH of the malate would be released as carbon dioxide. The label in the α-COOH group

Table 2. Distribution of Carbon-14 in Malic Acid and in the Glucose Moiety of Sucrose from Sunflower Cotyledons which had been exposed to Carbon-14 Dioxide for 15 min. in the dark

Glucose		Malic acid	
—CHO	5·2	—COOH	30·5
—CHOH	4·2	—CHOH	1·9
—CHOH	35·7	—CH_2	1·6
—CHOH	48·6	—COOH	66·0
—CHOH	3·0		
—CH_2OH	3·3		
	100·0		100·0

Values expressed as percentages.

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would be retained in the pyruvate or phosphoenol pyruvate and incorporated as carbon atoms 3 and 4 of the hexoses. Broadly the isotopic distribution reported for the glucose moiety of sucrose in Table 2 provides support for the reactions outlined. Since quantitative physiological studies[1] have demonstrated that, at the same stage of seedling growth, the fatty food reserve in the sunflower cotyledons is being rapidly converted into sucrose, a possible inference is that malate is an intermediate in this fat into carbohydrate conversion.

The glyoxylate cycle of Kornberg and Krebs coupled with a pathway such as that mentioned for the conversion of malate into sugar provides a possible mechanism for the conversion of fat into sugar in sunflower cotyledons. The enzymes relevant to the glyoxylate cycle, shown by Kornberg and Beevers to be present in castor-bean seedlings, have recently been demonstrated in cell-free preparations from the cotyledons of germinating sunflower and peanut seedlings[6]. In addition, feeding experiments with radioactive acetate have provided evidence for the operation of this cycle in the intact cotyledons[6,7]. The operation of the cycle in the cotyledons used in the present experiments could account for the spread of the carbon-14 label from the β-COOH group to the α-COOH group of the malic acid (see Table 2).

The metabolic significance of the incorporation of carbon-14 dioxide into the sunflower cotyledons in the dark is at present unknown. Clearly it may have resulted either from a net uptake of carbon dioxide by the tissue or simply from such incorporation as presumably occurs in any system normally in equilibrium with an atmosphere containing carbon dioxide when carbon-14 dioxide is introduced into that atmosphere. The low respiratory-quotient values (0·5–0·6) which have been observed[1] in 5-day-old sunflower seedlings could result from fixation of carbon dioxide, but can also be explained in terms of the operation of the glyoxylate cycle.

Acknowledgment is due to Prof. M. Thomas and Dr. S. L. Ranson for their helpful guidance and advice, and to King's College, in the University of Durham, for financial support.

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EFFECT OF GROWTH SUBSTRATES ON ISOCITRATASE FORMATION BY *PSEUDOMONAS OVALIS* CHESTER

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ISOCITRATASE, which catalyses the aldol cleavage of isocitrate to succinate and glyoxylate[1–3], is thought to play an essential part in the biosynthesis of cell constituents by micro-organisms growing on acetate as sole carbon source[4–9]. The levels of isocitratase found in bacterial extracts vary widely with the substrate on which the cells are grown[10] (Table 1), suggesting that the enzyme operates only when net formation of C_4-compounds from acetate is necessary for growth. This was tested by incubating a washed suspension of *Pseudomonas ovalis* Chester, which had been grown on acetate as sole carbon source[6], in growth media containing either 50 m*M* acetate or 50 m*M* succinate as carbon sources. Growth of the organisms was followed nephelometrically. At known times, samples of the growing cultures were centrifuged, suspended in 10 ml. of 0·9 per cent potassium chloride, disintegrated by supersonic vibration (at 25 kc./s., generated by a 600 W. Mullard magnetostrictor oscillator at 3·5 amp.) for 2 min., and centrifuged for 15 min. at approximately 20,000*g*. The isocitratase activity of the supernatant solutions was determined by a modification of the method of Olson[11], by measurement in a Cary recording spectrophotometer of the rate of change of optical density at 252 mμ, consequent upon the formation of glyoxylate semicarbazone, when cell extracts were incubated at *p*H 6·0 with semicarbazide and isocitrate.

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Table 1. Specific Activity of Isocitratase in Extracts of *Pseudomonas ovalis* Chester grown on different Substrates

Growth substrate	Specific activity (μmoles of glyoxylate formed/mgm. protein/hr.) at *p*H 6·0
Acetate	2·78
Glucose	< 0·01
Citrate	0·13
Succinate	0·25
Malate	0·15
Fumarate	0·06
Lactate	0·11
Alanine	0·09
Aspartate	0·08
Glycine	0·14
Glycollate	0·08

Cells used for inoculations of growth media had been maintained on 50 m*M* acetate medium (ref. 6) solidified with 2 per cent agar. Growing cultures were harvested at the approximate mid-point of logarithmic growth and washed with 0·9 per cent potassium chloride. Cell extracts were prepared as described in the text. Isocitratase was estimated spectrophotometrically, by the rate of change of optical density at 252 mμ due to the formation of glyoxylate semicarbazone, in the assay procedure of Olson (ref. 11). The identity with glyoxylate semicarbazone of the material absorbing ultra-violet was confirmed by preparation of the 2,4-dinitrophenylhydrazone from it after the assays, and identification of this derivative by paper chromatography (ref. 13). In all cases, glyoxylate was the only keto compound formed.

The results obtained (Fig. 1) show that these cells grown on acetate contained isocitratase at high specific activity at zero time, and that, when placed in fresh acetate growth medium, the isocitratase continued to be formed at a rate parallel to the formation of cell material. The cells placed in succinate growth medium, which initially contained isocitratase

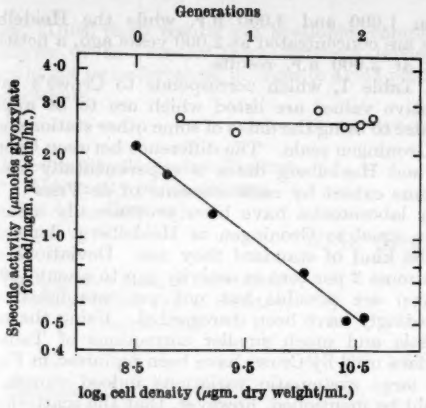

Fig. 1. Variation of specific activity of isocitratase with cell growth. *Pseudomonas ovalis* Chester grown on acetate, incubated in growth media containing 50 m*M* acetate (○—○) or 50 m*M* succinate (●—●) as sole carbon sources

at similar high specific activity, did not continue to form isocitratase, and the specific activity of the enzyme under these conditions of growth fell sharply with increasing cell density (Fig. 1). Under these conditions, the specific activity of the isocitratase decreased by 50 per cent in each cell generation, indicating that the apparent loss of enzyme activity was not due to destruction of the enzyme, but to 'diluting out' during growth.

Cells which had been grown on succinate as sole carbon source initially contained low levels of isocitratase activity (Fig. 2). When such cells were allowed to grow in a medium containing 20 m*M* succinate and 50 m*M* acetate (Fig. 2), the specific activity of the isocitratase remained low and constant despite an increase in the cell density from 0·50 to 1·80 mgm. dry wt./ml. of medium. The plot of the logarithm of cell density against time was linear (mean generation time 1·2 hr.) and showed no evidence of diauxie. Since manometric experiments had shown that cells grown on succinate oxidize acetate without lag, and since the amount of growth observed could not have been supported by 20 m*M* succinate, it must be concluded that the cells were utilizing for growth both the added succinate and acetate simultaneously. Only after the succinate in the medium was exhausted (after a cell increase of two generations) was an increase in the isocitratase level of the cells detected. Cells grown on succinate, placed in 75 m*M* acetate growth medium (Fig. 2), grew only after a lag of approximately 2 hr. During this time, the isocitratase-level rose sharply; the specific activity of the enzyme increased from 0·20 to 1·46 μmoles of glyoxylate formed/mgm. protein/hr. before any growth was detected. By the time the cell density had increased by a third of a generation, the specific activity of 2·7, observed in acetate-grown cells (Fig. 1), had been reached, and was maintained through the subsequent logarithmic growth (mean generation time 1·4 hr.). These results indicate that: (*a*) the formation of isocitratase by *Pseudomonas ovalis* Chester varies with the growth substrates used; (*b*) high levels of isocitratase are formed when a necessity exists for net formation of C_4-compounds from acetate, but the provision of such C_4-compounds in the growth medium represses[12] isocitratase formation; (*c*) the formation of isocitratase precedes growth on acetate. This supports the role of the glyoxylate cycle[4-9] as the route for biosynthesis of cell constituents from acetate; (*d*) isocitratase formation is not induced by acetate in the presence of a C_4-compound. It is possible that it may be elicited by a fall in the intracellular concentration of a repressor[12] (such as an intermediate of the tricarboxylic acid cycle), as would occur with the provision of acetate as sole carbon and energy source.

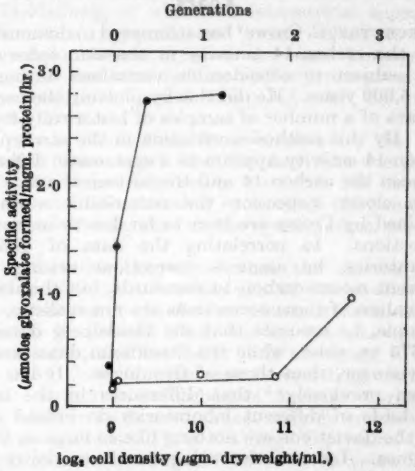

Fig. 2. Variation of specific activity of isocitratase with cell growth. Succinate-grown *Pseudomonas ovalis* Chester incubated in growth media containing 75 m*M* acetate (●—●) or 20 m*M* succinate + 50 m*M* acetate (○—○) as carbon sources

We wish to thank Sir Hans Krebs for his encouragement and interest, Prof. D. D. Woods for the gift of a culture of *Pseudomonas ovalis* Chester, Prof. Boris Magasanik (Harvard Medical School) for many stimulating discussions, Dr. H. B. Vickery (Connecticut Agricultural Experiment Station, New Haven) for a generous gift of potassium dihydrogen L$_S$-isocitrate, and Dr. June Lascelles for valuable help in the microbiological procedures used. This work was supported by the Rockefeller Foundation and by the Office of Scientific Research of the Air Research and Development Command, U.S. Air Force, through its European Office, under Contract No. *AF*.61(514)-1180.

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LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications.

Carbon-14 Activity during the Past 5,000 Years

Recently, C. Crowe[1] has attempted to demonstrate that the carbon-14 activity in the atmosphere has been subject to considerable variations during the past 5,000 years. He did this by plotting the carbon-14 data of a number of samples of historically known age. By this method a variation in the atmospheric carbon-14 activity appears as a systematic difference between the carbon-14 and the historical age.

On closer inspection the remarkable variations obtained by Crowe are seen to be due to unjustified corrections. In correlating the data of different laboratories, he assumes corrections arising from different recent carbon-14 standards, but the numerical values of these corrections are not realistic. For example, he assumes that the Heidelberg dates are all 375 yr. older, while the Stockholm dates are 525 yr. younger, than those of Groningen. It has been shown previously[2,3] that differences in the recent standards of different laboratories do indeed exist, but the deviations are nothing like so large as Crowe assumes. Laboratories using wood standards from the previous century and others using modern organic material (from about 1930–53) give different ages for the same sample because of the effect of industrial combustion. This has the consequence that modern material and a standard derived from it show a lower activity. The latter group of laboratories accordingly give dates which are too young.

When this effect was discovered by Suess[4], some laboratories already working (for example, Chicago and Groningen) kept their modern standard for the sake of simplicity and intended to ascertain the exact value of the correction before applying it. Thus the Groningen dates are about 240 yr. later than the Heidelberg dates. On the other hand, a large deviation between Stockholm and Heidelberg cannot exist because both laboratories use pre-industrial wood. This has also been established experimentally by dates (unpublished) obtained for the same specimen. It is not quite clear to us how the large corrections found by Crowe arise, but it might be possible that they come from the fact that there are only a few carbon-14 dates of the same specimen made by different laboratories and that some of these dates have large statistical errors. The comparison of such dates will give a 'correction' having a considerable chance deviation, which then will enter the further calculations as a systematic one and seriously affect the results. Indeed, the variations of activity found by Crowe arise essentially from the corrections he applied to the Heidelberg and Stockholm dates, pushing the former up and the latter down. Because of the fact that the Stockholm dates cover the age-range between 1,000 and 3,000 B.P. while the Heidelberg dates are concentrated at 2,000 years ago, a fictitious peak at 2,000 B.P. results.

In Table 1, which corresponds to Crowe's table, tentative values are listed which are to be applied in order to bring the dates of some other stations on to the Groningen scale. The difference between Groningen and Heidelberg dates is experimentally known to some extent by measurements of de Vries[2]. The other laboratories have been provisionally assumed to be equal to Groningen or Heidelberg, depending on the kind of standard they use. Deviations of 1 or at most 2 per cent in activity (up to about 150 yr. in age) are possible but not yet established and accordingly have been disregarded. Using the more realistic and much smaller corrections of Table 1, the data used by Crowe have been replotted in Fig. 1. The large systematic variations indeed vanish. It should be mentioned, however, that the scattering of the points, though much smaller than before, is somewhat larger than to be expected from the root-mean-square counting errors alone. This may be due to the fact that data have been used which do not satisfy the necessary requirements as regards purity and reliability of historical evidence.

Table 1. Years to be Added to or Subtracted from all Dates to Bring them on to the Groningen Scale, which is not Corrected for the Suess Effect

University of Chicago	0
Institute of Archæology	0
Lamont Geological Observatory	−240
University of Michigan	−240
Swedish Geological Survey	−240
University of Heidelberg	−240

Tentative values are given here, the estimated root-mean-square error being ± 80 yr. For the Heidelberg value (−240) the root-mean-square error is smaller (± 40 yr.).

At this stage it can be seen, however, that genuine variations in carbon-14 activity, if present, are almost one order of magnitude smaller than those found by Crowe. In any event, plots of the kind in question will be more reliable as soon as the differences in recent standards are measured more exactly. This is at present being done by measuring standard organic material distributed by the U.S. National Bureau of Standards, Washington, and an artificial standard of higher activity distributed by the Heidelberg labora-

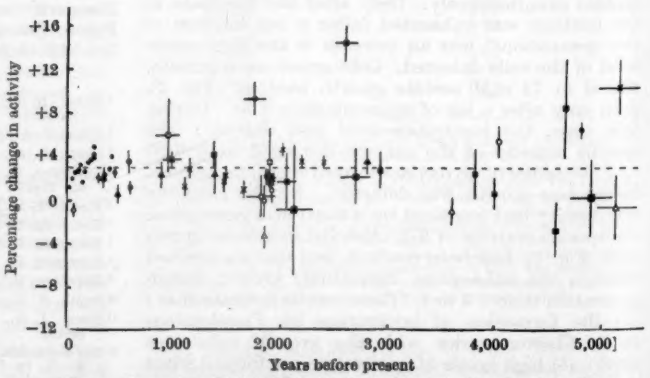

Fig. 1. Change in activity relative to that of the present versus time, taken from Crowe, but with the corrections given in our Table 1. (No attempt has been made to identify or to check the individual points; all points attributed by Crowe to each laboratory have been shifted as a whole.)

●, Groningen; ○, Heidelberg; △, Institute of Archæology; ▲, Lamont; □, Michigan; ×, Stockholm; ■, Chicago

tory. Until these results are available, comparative analysis of the results from different laboratories should not be undertaken, in order to avoid premature conclusions.

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IN a recent communication, C. Crowe[1] uses published dates on samples of known age in an attempt to investigate variations of the concentration of carbon-14 in living material during the past 5,000 years. He concludes that the activity has followed a cycle with a maximum change of 10 per cent and with some evidence of a sharp peak of about 10 per cent about 2,000 years ago. His proposed curve is most striking, for the effect, if real, would imply, for example, that all 1,000-year old samples should give radiocarbon ages of more than 1,700 years, a result which has not yet been obtained in practical measurement despite the growing number of accurate measurements on tree rings and other materials of known age.

Crowe assumes in the first place that the observed difference between the radiocarbon age and the known age of a sample is due entirely to the initial carbon-14 activity of the sample being different from that of present living material. This would only be justifiable if all other errors could be shown to have been taken into account, and if the statistical error of the radiocarbon estimation were small compared with the difference between the two ages. This is manifestly not so. Laboratories have differed to some extent in the past in dealing with the errors associated with radiocarbon dating, at first taking into account only the statistical errors of the radioactivity measurements; more recently, as other contributory factors have been discovered (for example, isotopic fractionation effects) these have been taken into account or eliminated when the necessary ancilliary instrumentation was available. Errors arising from the history of the sample before it enters the laboratory or from the lapse of time between the death of the sample and the event being dated are not included, although it is recognized that these effects, which are not amenable to mathematical treatment, may on occasion assume significant proportions compared with the statistical errors.

Secondly, Crowe attempts to eliminate systematic errors by comparing the ages obtained in the cases where laboratories have dated the same sample. This again is open to grave objection on the grounds that there are so few published examples available for such comparisons; no sample is common to all the laboratories mentioned, and in practically all cases the statistical errors are large compared with the observed differences, and thus it is very difficult to understand how his Table 1 was compiled. The only accurate approach to this problem of the elimination of systematic errors is that which is taking place at present and is being sponsored by Dr. K. O. Münnich of Heidelberg, in which all laboratories engaged in radiocarbon research are being asked to make extended measurements on the same homogeneous sample so that statistical and other errors are reduced to a very small value compared with the normal dating error.

Crowe's Table 1 is thus valueless on the above grounds alone, apart from the fact that one finds it difficult, if not impossible, to relate the values he quotes and the estimated error of $\pm$ 100 years with the available figures in the publications cited by him.

It is doubly important that the accuracy and validity of these corrections should not be allowed to go unquestioned. In the first place, one must at least attempt to prevent their use by the unsuspecting archæologist, and secondly, it is necessary to point out that Crowe's conclusions regarding the large cyclic variations in carbon-14 activity during the past 5,000 years depend almost entirely on the use of these corrections. Thus, the large depression in the trend line in the range of 1,000–2,300 years is due in the main to the influence of a group of Lamont and Stockholm samples which would occupy a much higher position nearer to the zero line were it not for the very large corrections applied to them by Crowe. Similarly, the evidence of a sharp peak at about 2,000 years seems to rest mainly on the large correction applied to the Heidelberg dates.

A more important point is that de Vries[2] has recently shown that the 'modern' standard in use in Groningen is 3 per cent lower in carbon-14 activity than the average for German trees and that consequently all Gröningen dates are in fact about 240 years too young. Crowe would have us believe that Lamont and Michigan dates are all 400 years younger, and Stockholm dates 525 years younger, than Groningen dates, and that therefore corrections of some 700 and 825 years respectively are required to convert results from these laboratories into calendar years. It is unlikely, to say the least, that three laboratories could be set up independently of each other and pass through the necessary proving and checking phases without detecting discrepancies of this magnitude.

Variations of carbon-14 activity during the past are clearly of importance to radiocarbon dating. It is known that they exist, but certainly at a lower order of magnitude than is implied by Crowe's calculations. The accurate approach to the problem of their evaluation is clearly an extension of the work of Münnich[3] and de Vries[2].

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A 'Solid-Image' Microscope

For many purposes, such as tracing networks of neural structure in the brain, a normal microscope has the serious limitation that only a thin layer of the specimen can be studied at one time, owing to the limited depth of focus of microscope objectives. When a thin section is examined, only those structures which happen to lie in the plane of the section can be observed. This plane may be confused by such objects as fibres coming away from or toward the plane of the section. A microscope which gave a large depth of field, and which presented the image as a solid in a luminous block in which the structures could be observed in depth would have important advantages over existing optical microscopes. We have designed and constructed a primitive prototype of an instrument giving such a 'solid image'. It is possible to observe this from any position and to see the structures with appropriate parallax.

The instrument involves two processes. (1) The focal plane of the objective is effectively made to 'scan' up and down through the depth of the section. In the prototype instrument, this occurs at a rate of 50 double scans/sec. The slide is mounted on a steel fork tuned to 50 c./s. which is driven by a polarized solenoid energized by a 50 c./s. sine wave. Thus the slide is carried up and down through the focal plane of the objective 50 times/sec. (2) The image is projected on to a screen mounted on a second tuned fork which vibrates at the same rate and in the same phase as the slide carrying the specimen.

Scanning serves to extract the information in depth from the specimen; the second process reconstitutes it in depth, giving a 'solid image' in the space swept by the screen. Its frequency of vibration is greater than the fusion frequency for the eye, so that little or no flicker is observed.

As the instrument stands at present, the resolution and contrast leave much to be desired. A test slide of human hair does, however, give a fairly satisfactory 'solid image' in which the positions of the hairs may be seen in depth. These positions change as the observer changes his viewing position. If the objective is brought farther from, or closer to, the slide the image of the test hairs moves through the luminous cube in a convincing manner. So far, magnifications greater than 100 have not been attempted, and the greatest useful magnification is only about 20.

We hope to produce an improved version, using the same basic principles but perhaps abandoning the physical screen in favour of shifting the virtual image of viewing lenses. The tuned forks may be replaced by some more precise system for obtaining the 'scanning' oscillatory movements. We intend to modulate the light intensity in order to increase the illumination inside the image. At present the front and back are brighter than the middle, because the velocity of the screen is greater at the centre of its sweep.

It is hoped that an instrument might be developed along these lines which will be useful for biological and other research purposes.

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Oct. 16.

Evidence for $^4_2$He 'Clusters' in Nuclei

The well-known 'α-particle' model of the nucleus, whereby certain low-A nuclei are considered as consisting of groups of α-particles, has recently received a new impetus as a result of work by Wildermuth and Kanellopoulos[1] on the 'cluster model' of nuclei. These authors have presented a formal treatment of the behaviour of 'cluster states' and illustrated it with particular reference to the nucleus $^8_4$Be considered as two α-particle clusters. At the same time they have pointed out that clusters other than $^4_2$He might be present, and in fact suggested that stable closed shells such as those with neutron numbers, N, of 50 and 82, could be considered as large clusters. The question now arises as to which clusters are in fact suitable representations of particular nucleonic configurations, and the purpose of this communication is to present evidence in this connexion.

This evidence is obtained from a simple study of the neutron numbers, N, and atomic numbers, Z, of stable nuclei. If clusters are in fact entities inside the nucleus, one would expect the $(N - Z)$ systematics of stable nuclei to show a tendency for stable nuclei to be separated from each other by the subnuclear clusters. That such tendencies do in fact exist can be seen from the published work of one of us[2,3], and we present here further evidence by way of illustration. Fig. 1 is an $(N - Z)$ versus Z diagram on which the stable even-Z odd-N nuclides have been plotted. The following features emerge very clearly: (*a*) In the low-Z region the stable nuclides are separated from each other by steps of $^4_2$He. (*b*) For higher-Z (44–56) the separation is in steps of $^6_2$He and not $^4_2$He. (*c*) The sequences are interrupted by the 'magic numbers'.

It should be mentioned that the region Z 16–44 has been omitted in order to preserve clarity in presentation. In most of this region separations of both $^4_2$He and $^6_2$He appear—it may therefore be regarded as some sort of intermediate region.

If now the $^4_2$He steps in the low-Z region are taken as evidence of the presence of $^4_2$He clusters in low-mass nuclei (as indeed seems reasonable), then it appears likely that $^6_2$He clusters are present in certain nuclei of higher mass. The same effect obtains, although not so strikingly and with less clarity, if one plots stable odd–even or even–odd nuclides (see, for example, ref. 3, Fig. 3, and ref. 2, Fig. 19).

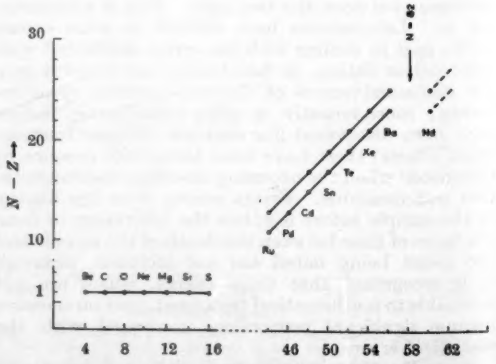

Fig. 1. $(N–Z)$ vs. Z diagram of stable even-Z, odd-N nuclides. The 'missing' nuclide $^{107}_{46}$Pd is very long lived with a half-life of 7×10^6 years

The evidence can be summarized as follows: (*a*) α-particle clusters appear to exist in the low-Z nuclei ($Z \ll 16$); (*b*) most of the region Z 16 to Z 44 appears to be a transitional region where the cluster can be either $^4_2$He or $^6_2$He; (*c*) from Z 44 to 56, $^6_2$He clusters appear to exist; (*d*) it seems likely that 'magic numbers' of protons or neutrons act as large clusters.

On this basis, then, one can (for some purposes, in any event) consider nuclei as consisting largely of 'closed shell' clusters plus one or more (seven appears to be a maximum number) smaller clusters of either $^4_2$He or $^6_2$He. If this is correct, it is, of course, most interesting to note that a cluster need not necessarily be an entity which is stable in itself ($^6_2$He is unstable with a half-life of 0·8 sec.). A rough parallel to this situation exists in the neutron; although the neutron is itself an unstable particle, it can apparently be considered to exist as an entity in nuclei.

The question of neutron excess should also be mentioned. $^4_2$He has, of course, zero neutron excess, whereas $^6_2$He has $(N - Z)$ equal to 2. The transition from $^4_2$He to $^6_2$He clusters is therefore probably necessary in order to provide an adequate neutron excess to balance the Coulomb repulsion at higher Z. It should be noted that the discontinuities at the shell numbers always result in a reduction in neutron excess; $^6_2$He clusters evidently provide rather too much neutron excess.

In the region $Z > 60$, $^6_2$He-type regularities are also present, and several additional points of interest arise. These will be included in a more complete discussion (at present in preparation) of the cluster regularities observable in stable-nuclide systematics. At the same time, an effort is being made to investigate whether other nuclear properties exhibit $^6_2$He cluster effects in the appropriate regions of atomic weight.

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Aug. 21.

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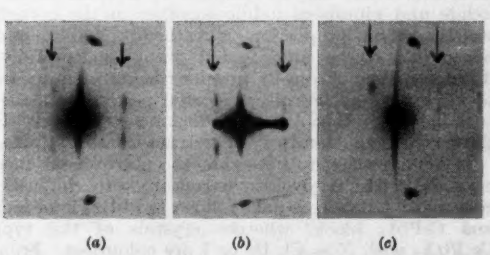
Extra Streaks in the X-ray Diffraction Pattern of Vanadium Single Crystals

Well-exposed Laue and oscillation photographs of vanadium single crystals show several streaks which can be easily distinguished from the Laue and Bragg spots and also from the diffuse areas of thermal scattering. Most of the following observations were made on specimens having at least one fairly bright (100) cleavage face of area 12–30 mm.[1]. The specimens were electropolished.

The lattice parameter was derived by two independent measurements. (1) Powder photographs taken with a crushed single crystal using copper $K\alpha$ radiation and a 19-cm. Unicam powder camera. This method gave $a = 3{\cdot}036 \pm 0{\cdot}002$ A. (2) The separation of 110 Kossel lines on the single crystal photographs. This method gave $a = 3{\cdot}035 \pm 0{\cdot}001$ A. Both values agree well with the precision measurements of Neuburger[1] on high-purity oxygen-free vanadium powder, who found $a = 3{\cdot}0338 \pm 0{\cdot}0003$ A. at 25° C.

The Laue and oscillation photographs were taken with copper $K\alpha$ radiation using a Unicam single-crystal goniometer fitted with a quarter-cylinder camera (radius 114·6 mm.) and a modified version of the half-cylinder camera (radius 57·3 mm.). The latter was capable of covering the angular range from $\theta = 0°$ to 77° along the equator. Collimators of diameter $\frac{1}{2}$ and $\frac{1}{4}$ mm. respectively were used. Ilford *G* X-ray film in a light-tight cellulose triacetate envelope was used. The envelope was covered with a nickel foil 0·020 mm. thick which served as a β-filter and also as an absorber of the fluorescent radiation generated in the specimen.

Powder photographs show nothing but fine continuous lines which may all be interpreted in terms of the body-centred cubic vanadium structure. The extra streaks (shown by arrows in Figs. 1,*a* and *b*) look similar to powder lines with strong preferred orientation. As the angle of incidence of the X-rays varies, the diffraction angles of the streaks remain constant, but their position along the 'powder lines' and their intensity change continuously. The intensity reaches its maximum near the centre of the angular range of incidence in which the streak is observable. This range of observability is 5°–6° for most streaks. For this reason the extra streaks on a Laue photograph and on an oscillation photograph taken around that particular stationary setting are similar (see Figs. 1,*a* and *b*). The streaks can thus be represented in reciprocal space by segments of concentric spherical shells around the origin of the reciprocal lattice. These segments subtend an angle of 5°–6° at the centre of the reflecting sphere and have maxima of intensity at their centres. Stationary-crystal photographs were taken in which the glancing angle of incidence of the X-rays on the (100) face was varied from 1° to 50°. In this angular range ten spherical shells were found and the radius of any given shell was the same for all specimens. The number of observed segments varied from one shell to another but on any particular shell it was the same for most of the specimens. One specimen, however, was found which showed a higher number of segments on some of its shells than did the other specimens. This particular crystal also behaved differently in another respect. For most specimens the arrangement of the segments on the shells conformed to the cubic symmetry of the whole crystal but the exceptional specimen showed a lower symmetry. This is illustrated by Fig. 1,*c*, which shows the extra streaks due to this specimen under the same conditions as for the usual specimens which gave Fig. 1,*a*. Fig. 1,*c* shows



(*a*) (*b*) (*c*)

Fig. 1. (*a*) Laue photograph taken at the 200 Bragg reflexion position with pairs of extra streaks on both sides of the Laue spot. (*b*) 5° oscillation photograph taken around the setting of Fig. 1,*a*. The extra streaks show no lateral shift. (*c*) Same as 1,*a*, but taken with the crystal which showed a greater number of extra streaks (see right-hand group). This photograph shows a horizontal plane of symmetry passing through the Laue spot for the positions, but not the intensities, of the extra streaks

the extra streaks in the same positions but the intensities are different from those of Fig. 1,*a*.

A detailed study of the structural implications of the above findings and their possible interpretation is in progress, and the results will be published elsewhere.

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[1] Neuburger, M. C., *Z. Kristallogr.*, **93**, 314 (1936).

Crystal Structure and Photoconductivity of Cæsium Plumbohalides

Wells[1] and his collaborators have shown that crystals of the general compositions $CsPbX_3$ with X = Cl, Br or I, and Cs_4PbX_6 with X = Cl or Br, may be prepared from aqueous solutions. I have investigated the structures of these crystals and also prepared a few more. I have found[2] that $CsPbCl_3$ and $CsPbBr_3$ have the perovskite structure. At room temperature they are tetragonally or monoclinically distorted. Both of them, however, show transition to pure cubic perovskite structure, at 47° C. and 130° C. respectively and with cell dimensions $a = 5{\cdot}605$ A. for $CsPbCl_3$, $a = 5{\cdot}874$ A. for $CsPbBr_3$. Whereas no extra or forbidden X-ray reflexions can be observed above these transition temperatures, $CsPbBr_3$ below 130° C.—and presumably also $CsPbCl_3$ below 47° C.—exhibit a new structure corresponding to a doubling of the cell dimensions. The transitions are likely to be of second order as $\Delta V = 0$ within the limits of accuracy of my measurements.

The $CsPbI_3$ crystals from aqueous solution are orthorhombic with space group No. 62 *Pnma* and $a = 4{\cdot}795$ A., $b = 10{\cdot}45$, A., $c = 17{\cdot}76$ A. The X-ray analysis yields all the atomic positions and interatomic distances: the lead atom is surrounded octahedrally by six iodine atoms at distances 3·01–3·42 A., and nine iodine atoms form distorted ditrigonal pyramids around each cæsium atom at distances of 3·87–4·19 A. The lead and iodine ions form chains of polynuclear complex ions parallel to the *a*-axis of the crystal. On heating these crystals to 305–308° C. they undergo a phase change and the colour changes from yellow to black. This black form which may also be obtained by melting cæsium iodide and plumbous iodide together in the correct stoichiometric proportion is rather unstable, and hence had to be investigated on a Geiger–Müller diffractometer. From its powder diagram it appears to have a monoclinically distorted perovskite structure ($a = b = 6{\cdot}15$ A., $c = 6{\cdot}23$ A., $\beta = 88{\cdot}15°$). It shows the same kind of superstructure as $CsPbBr_3$.

It is interesting to note that the above-mentioned crystals with perovskite structure are intensely coloured: $CsPbCl_3$ is pale yellow, $CsPbBr_3$ is orange and $CsPbI_3$ black, whereas crystals of the type Cs_4PbX_6 with X = Cl, Br or I are colourless. From this peculiarity one might guess that the former crystals also have special electrical properties. With a very crude apparatus we have found that the coloured $CsPbX_3$-crystals with perovskite structure are photoconductive, $CsPbCl_3$ having its maximum spectral sensitivity in the violet, $CsPbBr_3$ in the blue to green region and $CsPbI_3$ in the red region, that is, the spectral region which is complementary to the colour of the crystals.

A detailed account of this work will be published elsewhere.

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[1] Wells, H. L., *Z. anorg. Chem.*, **3**, 195 (1893).
[2] Møller, C. K., *Nature*, **180**, 981 (1957).

Nuclear Magnetic Resonance in β-Brass

Bloembergen and Rowland[1] have shown that the addition of small amounts of zinc to copper reduces the intensity of resonance in the resulting alloy so that the line becomes unobservable when the zinc content reaches approximately 25 per cent. They explained this effect in terms of quadrupole broadening and pointed out that, in ordered structures with cubic symmetry, quadrupole broadening should be absent and a line would be expected. However, they found no resonance in a β-brass of about 50/50 composition (quoted by Bridgman[2] as 47·3 per cent zinc) and they suggested that the ordering was not complete.

Experiments in this laboratory have shown that there is a strong copper-63 resonance in a β-brass containing 48·33 per cent zinc by weight. The specimens were prepared by filing at room temperature and sieving through a 120-mesh sieve, annealing for 2 hr. at 450° C. in an argon atmosphere, and then slowly cooling to room temperature. The detecting apparatus was a conventional Pound–Knight–Watkins type of spectrometer operating at approximately 5·96 Mc./s. and a 'Varian' 12-in. electromagnet set at approximately 5,250 oersted. All experiments were done at room temperature.

The main features of the resonance line for the annealed powder are as follows: (1) The line is symmetrical with the centre located 5·2 kc./s. below that for well-annealed copper of 99·98 per cent purity under the same conditions. This means that the Knight shift ($\Delta H/H$) for copper in a well-ordered β-brass structure is approximately 0·14 per cent, as compared with 0·23 per cent for pure copper. (2) The integrated area under the absorption line is one-sixth of the area under a line obtained from a specimen of pure copper containing the same number of copper nuclei. (3) The line for β-brass is appreciably narrower than that for pure copper, this smaller dipole broadening being consistent with the fact that the next nearest copper neighbours are farther away than they are in pure copper. (4) The line can be eliminated almost completely by plastic deformation. This was shown by testing a specimen immediately after filing and sieving.

The detailed effects of deformation, heat treatment, and variation of composition have been studied and will be described elsewhere.

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A New Phase in a Complex Alloy Steel

DURING investigations into the age-hardening of a steel containing 12 per cent chromium, 4 per cent nickel, 3 per cent manganese and 2·5 per cent silicon, a phase not previously reported was extracted electrolytically. This new constituent has been arbitrarily designated *S* phase.

Table 1. *d* SPACINGS OF *S* PHASE. LATTICE PARAMETER 11·50 A.

Intensity	*d* observed	*h,k,l*	*d* calculated
VVF	2·784	4,0,0	2·787
F	2·276	4,2,2	2·276
S	2·143	5,1,1 ; 3,3,3	2·144
VS	1·970	4,4,0	1·971
M	1·882	5,3,1	1·885
VF	1·858	6,0,0 ; 4,4,2	1·858
F	1·763	6,2,0	1·763
F	1·701	5,3,3	1·700
VF	1·680	6,2,2	1·681
VVF	1·487	6,4,2	1·490
VF	1·452	7,3,1 ; 5,5,3	1·452
F	1·315	8,2,2 ; 6,6,0	1·314
F	1·288	7,5,1 ; 5,5,5	1·287
M	1·224	9,1,1 ; 7,5,3	1·224
VVF	1·216	8,4,2	1·216
VVF	1·170	9,3,1	1·169
F	1·139	8,4,4	1·138
M	1·122	9,3,3 ; 7,7,1 ; 7,5,5	1·120
VF	1·079	9,5,1 ; 7,7,3	1·078
VF	0·9855	8,8,0	0·9856
F	0·9750	11,3,1 ; 9,7,1 ; 9,5,5	0·9741

Table 2

Element	Si	Ni	Mn	Cr	Fe
Atomic (per cent)	23·8	44·5	7·6	15·1	9·1

X-ray diffraction patterns and semi-quantitative chemical analysis revealed the structure and composition of *S* phase. The interplanar spacings are shown in Table 1. It has been indexed as a face-centred cubic lattice with parameter $a = 11{\cdot}50$ A. Table 2 gives the chemical composition of *S* phase. The values obtained suggest an approximate formula M_3Si, where *M* is largely nickel.

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A Method for Determination of Particle Penetration Depths in a Filter

A DETAILED knowledge of how particles penetrate a filter when an aerosol is filtered can give a good deal of information about properties of both filter and particles. In this communication, a simple method for the determination of particle penetration is described.

An aerosol, consisting of radioactive solid particles 0–2μ in diameter, was filtered at an air velocity of 100 cm./sec. through a glass-fibre paper (L.O.F. Glass Fibre Co., 475 Code 106 *AAA* glass, 0·2 mm. thick, 58 gm./m.^{2}, 'volume-surface' fibre diameter[1] 0·6μ).

225 cm.^{2} of this filter was pressed against a gummed cellulose-acetate film, with the air-entry side of the filter downmost. On removal, a thin layer of glass fibre was left on the sticky surface. The process was repeated until the whole filter was divided into twenty such layers each about 10μ thick. It was difficult to obtain layers of equal thickness, especially at the end of the process, when the sticky films now and then tore thicker pieces from the remaining glass-paper. The weights of the layers (after ashing of the sticky film) were found to vary between 30 and 80 mgm., the average being 60 mgm.

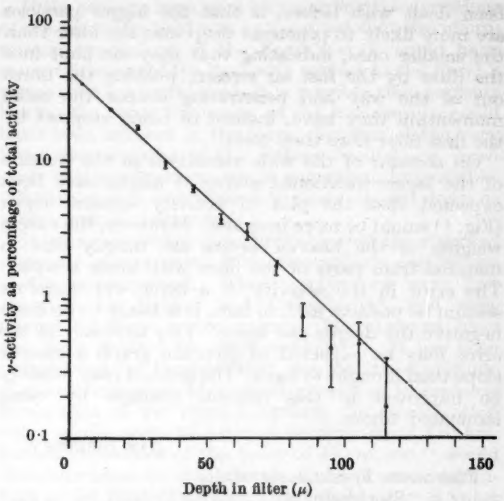

Fig. 1. γ-activity of filter layers as a function of depth in filter

Each layer was radioautographed and the γ-activity measured with a scintillation counter. The autoradiograph spots were counted and divided into five size classes, which were attributed to corresponding classes of radioactive strength by calibrating with active particles of known strength. The activity of the different particles being known, their sizes could thus be approximately determined.

The results are given in Figs. 1 and 2. An interesting phenomenon, which, so far as I know, has not

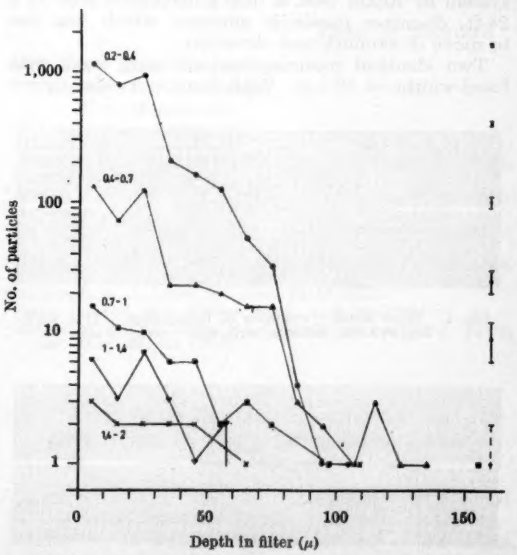

Fig. 2. Number of particles in filter layers as a function of depth in filter. The figures on the left are the range of particle diameters in μ. Statistical errors are given on the right

been dealt with before, is that the bigger particles are more likely to penetrate deep into the filter than the smaller ones, indicating that they are shot into the filter by the fast air stream, pushing the fibres out of the way and penetrating deeper the more momentum they have, instead of being stopped by the first filter fibre they meet.

On account of the wide variations in the weights of the layers mentioned above, it might have been expected that the plot of activity against depth (Fig. 1) would be more irregular. However, the excess weights of the heavier layers are mainly due to material from parts of the filter with lower activity. The error in the activity of a layer will therefore seldom be positive and, in fact, it is likely to be more negative the deeper the layer. This tendency of the error may be expected to give the graph a steeper slope than it ought to have. The method may possibly be improved in this respect, perhaps by using laminated filters.

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Comparison of Measured and Computed Values of the Rapid Fading-Rate of Ultra High-Frequency Signals reflected from the Moon

During August 1957, a bistatic moon reflexion experiment was carried out between South Dartmouth, Massachusetts (41·5395° N., 70·9512° W.), and Alpha, Maryland (39·3224° N., 76·9258° W.). The continuous-wave transmitter fed approximately 40 kW. of power, at a frequency of 412·85 Mc./s., into a horizontally polarized feed mounted in a 60-ft. diameter parabolic antenna. The antenna was movable in azimuth and elevation. The receiving system at Alpha used a dual-polarization feed in a 28-ft. diameter parabolic antenna, which was free to move in azimuth and elevation.

Two identical receiving systems were used, with band-widths of 50 c./s. With front end noise figures of approximately 5 db., maximum signal to noise ratios of approximately 25 db. were obtained. A common local oscillator was varied in frequency so that the changing Doppler frequency of the moon-reflected signal could be followed.

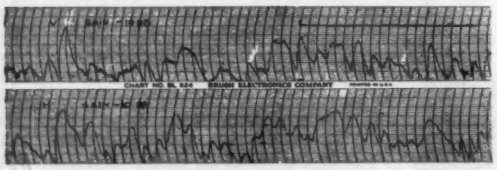

Fig. 1. Moon signal: examples of fading-rates. 1538 E.S.T. Top, vertical; bottom, horizontal. Scale, 10 sec.

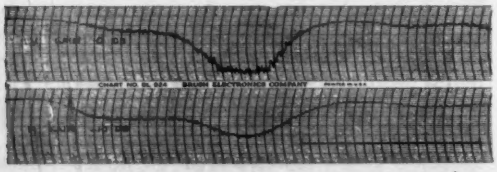

Fig. 2. Moon signal: examples of fading-rates. 0854 E.S.T. Top, vertical; bottom, horizontal. Scale 10 sec.

The system was operated from moonrise to moonset each day during August 6–August 29, 1957, apart from interruptions caused by equipment difficulties. The usual effects due to Faraday rotation were noted; that is, the individual signal-levels varied with periods of hours while the total received signal power-level remained quite constant, apart from the slow change due to the varying Earth–Moon distance.

The rapid fading-rate of the signals detected was observed to vary during the course of the experiment, from a maximum of several cycles per second to minimum rates at which the signal-levels remained almost constant for several minutes. Fig. 1 shows a typical fading-rate (with a detector time constant of 0·015 sec.), while Fig. 2 shows a very low fading-rate period.

It seemed reasonable to assume that the total effective libration rate of the Moon had a strong influence in producing these varying fading-rates[1]. For example, if the Moon is assumed to possess just three small reflecting regions, a central one and two others symmetrically located with respect to the centre, then a continuous wave signal would be reflected with small Doppler side-bands, in addition to the over-all Doppler shift. After detection, the side-bands would show up as effective 'fading' of the signal. Now in practice many portions of the Moon are effective in giving rise to appreciable reflexions, although a precise description of the mechanism is not possible. However, if on the Moon's surface one considers a circle drawn the radius of which is a given fraction of the full radius of the Moon, then one can examine all points on this circle and determine the maximum magnitude of the Doppler spread. By comparing this number with the observed fading-rate (defined in some rather arbitrary but consistent manner) it is then possible to determine whether or not the variations in fading-rate of the received signals are due primarily to a Doppler spread caused by libration.

A programme has been written for the *IBM* 704 computer which yields the over-all Doppler shift and libration-rate. Further trigonometry then enables these data to be converted into Doppler spread. Two subdivisions were made in the programme. (1) First-order differences only were retained, leading to a result which was normalized with respect to the Moon's radius. (2) Further refinements were introduced, leading to computations which could not be normalized, but which had to be carried out for a number of values of fractional radii of the Moon.

Results obtained from (1) are shown in Figs. 3 and 4, with a figure of 0·67 used for the fractional radius of the Moon. That is, the computed 'fading-rates' are actually computed maximum Doppler spreads on a circle of two-thirds the Moon's radius. The observed fading-rates were obtained by counting maxima of the detected signal over an interval of a minute or so at each period.

In general, results from (2) above were not significantly different from results obtained from (1). At periods of very low fading-rate the computed values from both (1) and (2) showed spreads of the order of 0·01 cycle per second, while the observed fading-rates often were considerably less than this.

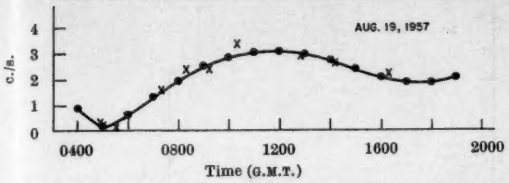

Fig. 3. Fading-rate of signal reflected from the Moon. ●, Computed; ×, experimental

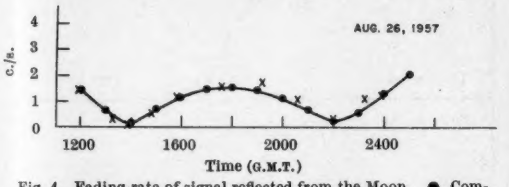

Fig. 4. Fading-rate of signal reflected from the Moon. ●, Computed; ×, experimental

It appears that the limiting factor in the accuracy of the computation is probably the somewhat abbreviated values of selenographic latitude and longitude, published in the American Ephemeris and Nautical Almanac. However, apart from the periods of very low fading-rate, excellent agreement was obtained between measured and computed values. Hence, for frequencies in the ultra high-frequency band, it appears that the rapid fading of a signal reflected from the Moon can be predicted in some detail from dynamical considerations. Thus other effects, for example, those which might be due to the ionosphere, must be correspondingly limited. Any extreme effect, such as that which might occur during auroral activity, might show up experimentally as a noticeable departure from the computed values.

It is a pleasure to acknowledge the assistance of the staff of the Massachusetts Institute of Technology Round Hill Field Station at South Dartmouth, Massachusetts, and many others in the Lincoln Laboratory who took part in the experiment.

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Possible Causes of Geomagnetic Fluctuations having a Six-Second Period

Geomagnetic fluctuations of two different types in the frequency-range 0·1–30 c./s. have recently been reported by Duffus *et al.*[1]. Fig. 2 of their communication shows that one of these types closely resembles two other naturally occurring oscillations, and has a period (about 6 sec.) of the same order as the latter. These two naturally occurring (and probably associated) oscillations are microseisms and microbaroms, and one or the other of them may be the cause of the observed magnetic oscillations.

If the pick-up loop used for recording the variations of the magnetic field was so mounted that the microseismic oscillations of the Earth's crust could have caused rotation of the loop with respect to the Earth's permanent magnetic field, it is possible that currents having the same frequency as the microseisms could have been induced in the loop. Because of the very large wave-lengths of the seismic oscillations, however, this explanation seems somewhat improbable. (The entire loop would tend to move up and down as a unit rather than rotate.)

It seems somewhat more probable that the observed magnetic effects result from atmospheric oscillations of the same period. These oscillations were first observed by Benioff and Gutenberg[2,3], and were named by them microbaroms. Microbaroms have also been studied by other workers[4–7]. It has been pointed out by Daniels[8] that the particle amplitude of microbaroms would be much greater at ionospheric levels than at the Earth's surface, the amplification being of the order of 1,800 at an altitude of 120 km. Particle velocities of the order of 40 cm. sec.$^{-1}$ would therefore occur at this altitude if the pressure amplitude at the Earth's surface were 1 dyne cm.$^{-2}$ (a value which is occasionally observed).

A detailed theory explaining how an atmospheric oscillation having such a period and velocity can give rise to a magnetic fluctuation still remains to be formulated. The relationship between the magnetic and microbarometric oscillations could, however, be studied experimentally by making simultaneous observations of the two phenomena. A similar study was made by Saxer[7] for the purpose of establishing a correlation between microbaroms, microseisms and ocean waves. One difficulty connected with such a study is that the microbarometric pressure variations are so small that they are often masked by pressure fluctuations due to atmospheric turbulence. This interference, however, could be minimized by using an infra-sonic line microphone of the type invented by Daniels[8] with which an improvement in the signal-to-wind-noise ratio of as much as 20 db. can be achieved at frequencies in the region of interest.

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Zeta Potential and Sedimentation Behaviour in Flocculated Cane Sugar Juice

The stability of an aqueous suspension is reflected in both sedimentation-rate and sedimentation-volume[1,2]. In a stable system, settling of the single particles is slow, but they remain free to move independently of each other into positions of close

packing in the sediment. In the unstable and flocculated system, settling of the particle aggregates is rapid, but their packing in the sediment is now of a random nature and the sedimentation volume is large. When the flocculation of a stable suspension is brought about by a decrease in zeta potential, both settling-rate and sedimentation-volume increase as ζ approaches zero.

When flocculation of the suspension is not brought about by a change in ζ, the particles within a floc still carry their original electrostatic charge. The question then arises: To what extent can a change in ζ now affect the sedimentation behaviour of the flocs?

Cane juice is a protein-stabilized suspension of waxy and other particles[2] which may be flocculated by the precipitation *in situ* of calcium phosphate; in this case complete destabilization occurs with no appreciable change in ζ. The flocs are composed of clusters of particles bound together in a matrix of the inorganic precipitate[4] and they settle to give a mud volume approximately twenty-five times the total volume of particles and precipitated material. It is therefore of interest to study the effect of a decrease in ζ upon the sedimentation of this unstable system in which flocculation is effectively independent of ζ.

Fig. 1 shows the effects on sedimentation and zeta potential of two detergents, cetyltrimethylammonium bromide and sodium laurylsulphate. The experimental method used to assess sedimentation behaviour has been fully described in another paper[5], where the calculation and significance of the settling constant K (the velocity of the interface when the volume of mud is twice that after infinite settling time) and the sedimentation volume H_∞ (the volume percentage of mud after infinite settling time) are fully discussed. Determination of electrophoretic mobilities was carried out by a microelectrophoresis technique fully described in another paper[6]. Mobilities could not be measured directly on settling-tube contents, but were measured on samples of juice diluted twenty-fold with 0·01 M potassium chloride in the required concentration of detergent. Since the sedimentation behaviour curves are symmetrical about the reversal of charge concentration of cetyltrimethylammonium bromide (0·37 mM) determined on these diluted samples it must be concluded that the same reversal of charge concentration would have been found in the settling-tube contents. Consistent with this observation, it may be noted that in oil/water emulsions stabilized by bovine serum albumin the reversal of charge concentration of myristyltrimethylammonium bromide is 0·36 mM and this value is independent of concentration of both total protein and oil drops (Bennett, M. C., and Haydon, D. A., unpublished work).

The outstanding feature of the sedimentation behaviour lies in the fact that there is a maximum in settling-rate at the reversal of charge point and that this is accompanied by a minimum in sedimentation-volume. The occurrence of a minimum in sedimentation-volume shows that the decrease in ζ has not led to an increase in particle aggregation, and it follows that the maximum in settling-rate must be attributed to a more closely packed arrangement of particles within the floc itself. On the basis of the floc structure described above it may therefore be suggested that mutual electrostatic repulsion between individual particles in a floc tends to maintain a less closely packed spatial arrangement than might be assumed

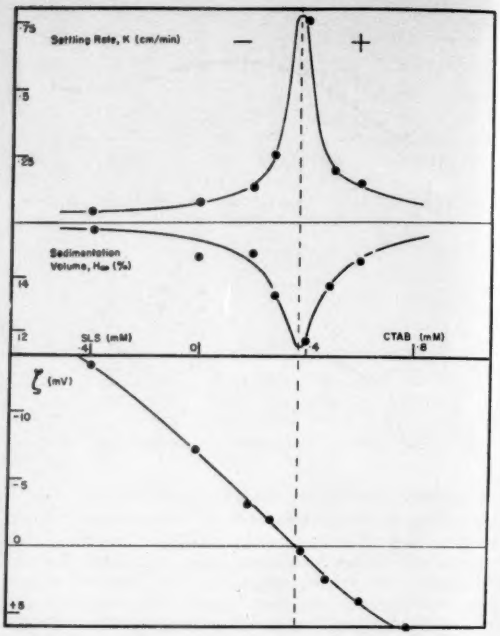

Fig. 1. Settling rate, sedimentation volume and zeta potential against concentration of cetyltrimethylammonium bromide (CTAB) and sodium laurylsulphate (SLS)

by uncharged particles. A decrease in particle charge should therefore lead to a more compact floc structure, which must be accompanied by an increase in settling-rate and a decrease in sedimentation-volume.

In similar studies on other cane juices it has been possible to demonstrate marked deviations from the behaviour described here. In one case, the H_∞ curve showed a slight maximum at the reversal of charge point; it was shown that this juice was abnormally stable towards calcium phosphate precipitation so that a reduction in zeta potential was accompanied by an appreciable decrease in stability and an improvement in flocculation. In some juices, the flocculated system was found to be completely insensitive to the action of detergents, while in others the reversal of charge concentration of cetyltrimethylammonium bromide was found to have increased to as much as 0·70 mM. In every case it is believed that these deviations are associated with the presence at the particle surface of layers of various polysaccharide materials; the evidence is discussed elsewhere[6].

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Colorimetric Determination of Inorganic Phosphorus in the Presence of Glucose-1-phosphate and Adenosine Triphosphate

THERE are many occasions in biochemical work in which inorganic phosphorus must be determined in the presence of some acid-labile phosphorus compounds such as glucose-1-phosphate or adenosine triphosphate. In Allen's method[1], for example, molybdenum blue colour is developed in 0·5 *N* perchloric acid. Owing to high acidity of the medium, glucose-1-phosphate or adenosine triphosphate is more or less hydrolysed during colour development and interferes with the determination.

During their studies on the mechanism of action of amylophosphorylase, Whelan and Bailey[2] found that hydrolysis of glucose-1-phosphate could be reduced to one-seventh as compared with Allen's original method by halving the specified amount of the reducing agent in colour development. It was interesting to re-examine their experiments for two reasons: (1) Although there are some reports[3,4] on the catalytic effect of molybdate on the acid hydrolysis of some acid-labile phosphorus compounds, there is no report pertaining to the effect of the amidol reagent. (2) Moreover, one of us[5] developed, several years ago, a modification of Allen's method, in which sulphuric acid was used in place of perchloric acid and the amount of the amidol reagent was halved. It was, at that time, not known that the amount of the amidol reagent might have some effect on the hydrolysis of glucose-1-phosphate. The amount of the amidol reagent was halved only because half the original amount was sufficient for most determinations and excess might better be avoided.

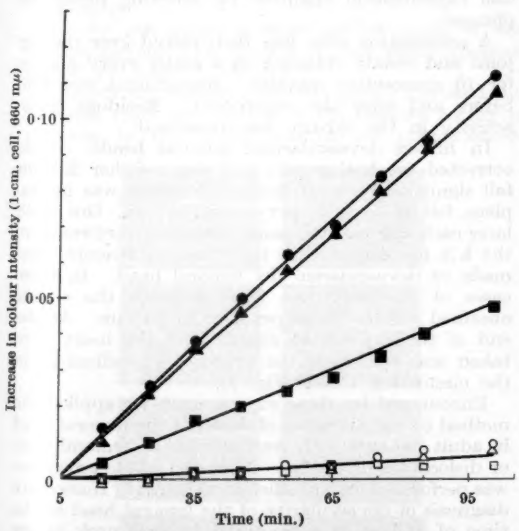

Fig. 1. Increase in intensity of molybdenum blue colour due to hydrolysis of glucose-1-phosphate. Circles, Allen's method—4·8 per cent perchloric acid, 0·08 per cent amidol, 1·6 per cent sodium bisulphite and 0·33 per cent ammonium molybdate. Triangles, Whelan and Bailey's modification—4·8 per cent perchloric acid, 0·04 per cent amidol, 0·8 per cent sodium bisulphite and 0·33 per cent ammonium molybdate. Squares, Nakamura's modification—1·5 per cent sulphuric acid, 0·04 per cent amidol, 0·8 per cent sodium bisulphite and 0·33 per cent ammonium molybdate. The reaction mixtures contained, in addition, 0·07 μmole of potassium dihydrogen phosphate and 1·14 μmoles of glucose-1-phosphate per ml. of the final solution. Open signs, colour developed at 18° C.; black signs, at 33° C. The colour intensity at 5 min. after colour development was arbitrarily taken as zero

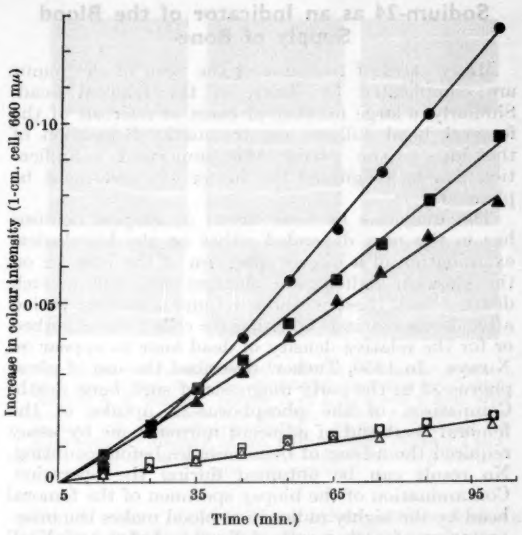

Fig. 2. Increase in intensity of molybdenum blue colour due to hydrolysis of adenosine triphosphate. The reaction mixtures contained 0·63 μmole of adenosine triphosphate per ml. in place of glucose-1-phosphate. Other additions and conditions are the same as in Fig. 1

Typical results of determinations of inorganic phosphorus by the three methods mentioned above in the presence of glucose-1-phosphate and adenosine triphosphate are shown in Figs. 1 and 2, respectively. In these figures, increase in colour intensity is plotted against time of colour development, the absorbancy at 5 min. after colour development being arbitrarily taken as zero. The amount of the amidol reagent has indeed some effect on the hydrolysis of glucose-1-phosphate and adenosine triphosphate when colour is developed at 33° C.; but the temperature at which colour is developed is a far more important factor. At 18° C., very little hydrolysis of glucose-1-phosphate or adenosine triphosphate occurs irrespective of the amount of the amidol reagent and the nature of the acid used. Although the acidity of the medium is approximately the same and hydrolysis of adenosine triphosphate is also the same in these three methods, the hydrolysis of glucose-1-phosphate at 33° is much smaller in sulphuric acid medium than in perchloric acid media.

Fructose-1,6-diphosphate and phosphoryl(enol)-pyruvate interfere less seriously with the determination of inorganic phosphorus by these methods.

Details will be published later (*Bull. Agric. Chem. Soc. Japan*).

We wish to express our sincere thanks to Prof. S. Funahashi for his interest in this work.

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Sodium-24 as an Indicator of the Blood Supply of Bone

Many cases of fractures of the neck of the femur are complicated by death of the femoral head. Similarly, a large number of cases of necrosis of the femoral head follows on traumatic dislocation of the hips. The earlier this important complication can be diagnosed the better can treatment be planned.

The diagnosis of bone death or aseptic necrosis has in the past depended either on the histological examination of a biopsy specimen of the bone or on the classical radiological changes that follow such death. Both these methods require a waiting period after devascularization, either for cells to be absorbed or for the relative density of dead bone to appear on X-rays. In 1950, Tucker[1] described the use of phosphorus-32 in the early diagnosis of such bone death. Comparison of the phosphorus-32 uptake of the femoral head and of adjacent normal bone by assay required the ashing of bone samples before counting. No result can be obtained during the operation. Contamination of the biopsy specimen of the femoral head by the highly radioactive blood makes the interpretation of such results difficult. Arden and Veall described similar studies[2]. Later, Bohr *et al.*[3] estimated the uptake of phosphorus-32 by inserting a probe Geiger counter into the femoral head. They recognized that counts could only be obtained from about a 1-mm. cylinder of bone around the probe, the β-radiation of phosphorus-32 being easily filtered out, even by soft tissue. No picture of the overall circulation in the femoral head could be obtained. Other workers have developed the use of sodium-24 clearance as an indicator of muscle circulation. In this method the rate of the fall in the local radioactivity due to sodium-24 injected in the muscle is used as an indication of its removal by the circulation. Advantages of this method include the short half-life of sodium-24 (15·06 hr.), giving clinical safety at the dose of 100–150 μc. used, and its 2·76 and 1·38 MeV. γ-photon emission which easily penetrates bone and soft tissues, making surface counting easy.

On attempting to apply this method to the investigation of bone circulation several difficulties were encountered. First, the labelled isotonic saline had to be introduced into a cavity in the bone without disturbing the local blood vessels unduly. Secondly, the syringe introducing the saline had to engage the bone firmly to prevent leakage of the radioactive material and thus a false fall of local radioactivity. At the same time the internal pressures developed in the femoral head in engaging the syringe should not interfere unduly with the patency of blood vessels inside the bone. A push-tight fit would thus not do. In co-operation with Mr. James Hite, of Zimmers Manufacturing Co., Warsaw, Indiana, a syringe was developed. It is all metal apart from the rubber O-rings used to obtain a watertight fit of the plunger in the barrel. A hole of small diameter in the end of the syringe allows easy emptying when the plunger is screwed home, while at the same time preventing premature escape of radioactive saline. A coarse Sherman type external thread with self-tapping flutes is provided at the end of the syringe to screw home gently but firmly in the femoral head.

Sterile isotonic saline containing 500 μc. sodium-24 per ml. was prepared. The largest obtainable dogs were used to reproduce conditions in the human so far as possible. Under full aseptic precautions and general anæsthesia the right hip of each dog was exposed and dislocated. The ligamentum teres was severed, and all vessels and periosteum were stripped from the femoral neck to devascularize the head of the femur so far as possible. A hole was then drilled up the femoral neck from the lateral cortex of the shaft into the femoral head. A small syringe loaded with approximately 0·1–0·2 ml. saline (that is, approximately 50–100 μc. sodium-24) was then screwed home until it had reached within $\frac{1}{4}$–$\frac{3}{8}$ in. of the end of the drill hole. The syringe was then emptied into this experimental chamber by screwing home the plunger.

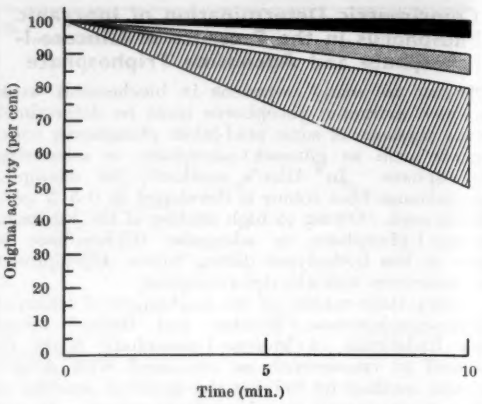

Fig. 1. Clearance of sodium-24 from dog femoral heads. Black, devascularized; stippled, partly devascularized; shaded, normal blood supply

A scintillation tube was then placed over the hip joint and counts obtained on a scaler every minute for 10 consecutive minutes. Background was read before and after the experiment. Residual radioactivity in the syringe was measured.

In fifteen devascularized femoral heads, counts corrected for background and decay either did not fall significantly or, if devascularization was incomplete, fell by up to 15 per cent in 10 min. One week later each dog had the same procedure performed on the left hip except that this time no attempt was made to devascularize the femoral head. In these cases of obviously live femoral heads the counts obtained fell by 20–50 per cent in 10 min. At the end of the experiment counts over the heart were taken and confirmed the presence of sodium-24 in the circulating blood (Fig. 1).

Encouraged by these experiments, we applied the method to the diagnosis of death of the femoral head in adult patients with fractures of the femoral neck or dislocation of the hip. Here the whole procedure was performed under radiological control. Immediate diagnosis of devascularity of the femoral head at the time of nailing of a fractured femoral neck allows the surgeon to alter his operation from a simple nailing to bone grafting and high femoral osteotomy or any other procedure he favours. The patient is thus spared a second operation aimed at the late treatment of avascular necrosis. In dislocation of the hip an immediate prognosis as to whether or not avascular necrosis is to be expected can be given.

Our thanks are due to Dr. Campbell Moses, under whose licence this work was performed, to Dr.

Russell Anderson, Mrs. Mary Grebner and Miss Patricia Orlic, for technical assistance, and to the U.S. Public Health Service for grant No. 1625.

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Effect of γ-Aminobutyryl-Choline upon the Electrical Activity of the Cerebral Cortex

Recently, Kuriaki[1] succeeded in synthesizing γ-aminobutyryl-choline and obtained some evidence of its presence in the brain. In the present study we have observed its effects on the electrical activity of the cerebral cortex.

Experiments were carried out on ten rabbits and a few cats under urethane anæsthesia. Evoked potentials were led off by means of a unipolar silver wire electrode with a ball tip (diam. 0·5 mm.) placed on the pial surface.

For electrical stimulation, square-wave pulses of 0·02–0·1 msec. were used. Shock artefacts were minimized by the use of an isolation transformer. Potentials were recorded by a condenser-coupled amplifier (time constant 0·5 sec.) led to a dual-beam oscilloscope.

All the test solutions were applied locally to the cortical surface with squares of filter paper approximately 2·0 mm. × 2·0 mm.

The primary sensory potential complex evoked and recorded from the surface of the sensory cortex in response to the stimulation of the contra-lateral peroneal nerve consists of an initial surface-positive potential followed by a surface-negative wave.

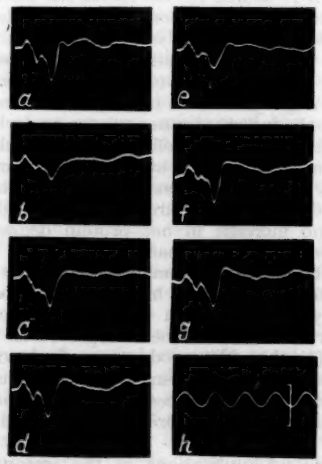

Fig. 1. Effect of γ-aminobutyryl-choline on the primary sensory potential evoked by stimulation of the contra-lateral peroneal nerve. Left-hand column: *a*, control; *b*, 30 sec. after the application of $4·0 \times 10^{-4}$ *M* γ-aminobutyryl-choline; *c*, *d*, respectively, 30 sec. and 5 min. after the cortex was washed with Ringer solution. Right-hand column: *e*, 3 min. after $4·0 \times 10^{-3}$ *M* γ-aminobutyryl-choline; *f*, *g*, recovery of responses 1 and 2 min. after washing off γ-aminobutyryl-choline; *h*, 50 c.p.s. The vertical bar represents 0·5 mV.

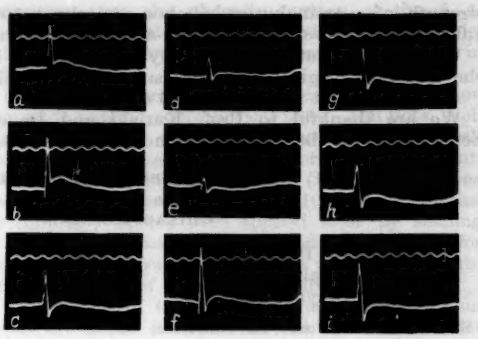

Fig. 2. Effect of γ-aminobutyryl-choline on the dendritic potential at 2 mm. distant from the stimulating electrodes in a rabbit. Records *a*, *b*, control; records *c*, *d*, *e*, 3, 4 and 6 min. after $4·0 \times 10^{-3}$ *M* γ-aminobutyryl-choline; record *f*, 2 min. after washing off γ-aminobutyryl-choline. Response increased for some minutes. Record *g*, 16 min. after washing; record *h*, 5 min. after $4·0 \times 10^{-4}$ *M* γ-aminobutyryl-choline; record *i*, recovery 1 min. after washing

Topical application of γ-aminobutyryl-choline to the sensory cortex resulted in rapid decreases in the surface-positive as well as surface-negative phase of the evoked potential.

The concentrations which caused appreciable depression were $4·0 \times 10^{-5}$–$4·0 \times 10^{-4}$ mol./l. An example is shown in Fig. 1. In addition, there was a prolongation of the surface-positive wave.

Depression of the primary sensory evoked potential occurred at once after the application. Washing the substance from the cortex resulted in rapid recovery (almost within 30 sec.) of the original wave form.

γ-Aminobutyryl-choline exhibited marked inhibitory action on the local electrical response of the cortex to direct surface stimulation. The response was led off at 2 mm. distant from the stimulating electrodes. γ-Aminobutyryl-choline was applied to the locus where the response was recorded.

With stronger stimulation, the direct cortical response consists of an initial surface-negative wave followed by a positive wave and a secondary surface-negative slow wave. γ-Aminobutyryl-choline depressed rapidly two surface-negative components, but left the surface-positive component almost unaffected for a few minutes. Using concentrations greater than $4·0 \times 10^{-5}$ mol./l., we observed the striking inhibitory action of γ-aminobutyryl-choline on the direct cortical response.

On washing the chemical from the cortex, immediate recovery took place; though an increase in amplitude of the initial negative component beyond the original was sometimes observed in the beginning phase of the recovery. A typical example is given in Fig. 2.

The inhibitory action of γ-aminobutyryl-choline on the metrazol-convulsive spikes was compared in the same rabbits with that of γ-aminobutyric acid, the inhibitory action of which on the electrical activity of the cortex has been reported by some investigators[2,3].

γ-Aminobutyric acid could induce complete inhibition of the excitation by 10 per cent metrazol in the concentration of $1·0$–$5·0 \times 10^{-1}$ mol./l. On the other hand, γ-aminobutyryl-choline, at $2·0$–$4·0 \times 10^{-4}$ mol./l., caused complete inhibition. That is, the inhibitory

strength of γ-aminobutyryl-choline was about 500–1,000 times as powerful as that of γ-aminobutyric acid.

We consider that γ-aminobutyryl-choline may be the true physiological inhibitory substance in brain.

A fuller account will be reported elsewhere.

We are thankful to Prof. Kuriaki and Daiichi Seiyaku Co. for the gift of γ-aminobutyryl-choline.

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Production of Glucose by the Liver during Hyperglycæmia

The effect of hyperglycæmia on hepatic glucose output has been studied employing an isotope dilution technique. Glucose labelled with carbon-14, of the same specific activity as the blood glucose, was injected in amounts sufficient to produce hyperglycæmia. The selection of the appropriate specific activity for this glucose 'load' was made easier by a procedure in which an infusion of labelled glucose (in 'weightless' amount) was continued throughout the experiment. During such an experiment the blood glucose specific activity remains relatively constant so long as the flow of unlabelled glucose from the liver continues at a uniform rate. On the other hand, the specific activity of the blood glucose rises if the flow of unlabelled glucose from the liver stops or decreases[1]. The present technique avoids the misleading values for plasma glucose specific activity which might result from slow mixing of injected unlabelled glucose with a labelled body glucose pool[1].

In two experiments in pentobarbital anæsthetized dogs, an amount of glucose with an appropriate specific activity was injected to produce hyperglycæmia (Fig. 1). During the period of hyperglycæmia the blood glucose specific activity did not rise. This indicates that the output of unlabelled glucose by the liver continued during the period of hyperglycæmia.

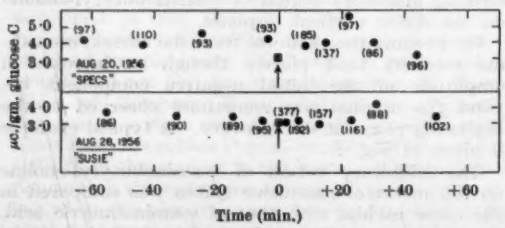

Fig. 1. Carbon-14 concentration in blood glucose before and after the injection of a glucose load and during a constant infusion of glucose-^{14}C in 'weightless' amount. The carbon-14 concentration of the glucose load, 1 ml. of 30 per cent (w/v) glucose/kgm. dog weight, is shown by the location of the × enclosed in a square at zero time (the mid-point of the load injection interval of 2–3 min. duration). Blood glucose concentrations in mgm. glucose per 100 ml. whole blood are given in parenthesis above or below each point showing carbon-14 concentration. Randomly labelled glucose-^{14}C was used in these experiments

These studies, therefore, do not support the conclusion[2,3], based on measurements of liver blood flow and differences of hepatic arteriovenous blood glucose concentration, that hyperglycæmia stops net hepatic glucose output. However, there is not necessarily a conflict between the present studies and these previous findings, since among the determinants of net hepatic glucose output are factors which are not measured by the isotope technique.

The uptake and output of glucose by the liver after a large amount of glucose is administered may involve several metabolic processes. Storage (whether in extracellular fluid, intracellular fluid or as preferentially removable end-groups of glycogen[4]) of blood glucose may occur during hyperglycæmia, followed by loss to the blood of the same glucose molecules as the blood glucose concentration returns to normal. In addition, during hyperglycæmia there may be increased utilization by the liver of circulating glucose for carbon dioxide production or for net synthesis of non-carbohydrate materials. These processes will influence the net difference between glucose entering and leaving the liver as determined by hepatic venous catheterization methods, but, there being no dilution by glucose-^{12}C, they will not be reflected in hepatic glucose production as measured by isotope dilution techniques.

The net production of new glucose molecules in the hepatic cell influences the measurement of net glucose output in catheterization studies and is thought to be almost entirely responsible for the decrease in specific activity observed in experiments employing isotopic tracer methods to determine hepatic glucose output. This process is of particular interest with regard to diabetes mellitus, because it has been implied[5] that insulin acts directly to stop hepatic glucose output during hyperglycæmia in the normal animal, whereas in the diabetic animal the absence of insulin eliminates this direct control mechanism.

It is conceivable also that an exchange of carbon-14 and carbon-12 atoms via the metabolic intermediates in the liver cell might contribute to a decrease in specific activity during isotope dilution measurements in certain circumstances. For example, an increased turnover of liver proteins during hyperglycæmia might introduce more carbon-12 atoms into the metabolic intermediates common to carbohydrate and amino-acid metabolism and simultaneously remove more carbon-14 atoms in the direction of protein synthesis. The end result would be a more rapid dilution of the circulating labelled glucose, whereas no increase in net protein degradation or net glucose production had occurred.

From the above it is concluded that the undiminished rate of dilution of labelled blood glucose during hyperglycæmia in the anæsthetized normal dog reported here must be interpreted as indicating either: (1) that the production of glucose in the hepatic cell continues during hyperglycæmia, or (2) if glucose production does cease there is a concomitant increase in an exchange process of the kind discussed above.

In previous applications of the isotope dilution technique to this question the results have been interpreted as indicating that hepatic glucose production ceases during hyperglycæmia[5,6]. In these earlier studies a glucose-^{12}C 'load' was administered after a single injection of glucose-^{14}C and considera-

tion was not given to the slowness with which intravenously injected glucose mixes with a part (about half) of the glucose pool.

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'Karathane' : the Relative Importance of the Phenolic and Unsaturated Acid Components in Toxicity towards Certain Plant Pathogens

THE commercial acaricide and fungicide currently offered as 'Karathane' has been shown to be one of the few substitutes for sulphur for the control of powdery mildews on a number of crops. The active ingredient is stated to be 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate, although some of the phenol is usually present in the free state.

Rich and Horsfall[1] reported that "laboratory and greenhouse tests showed that tenacity and phytotoxicity are due to the dinitrocaprylphenyl portion of the molecule, while the fungitoxicity is due to the crotonic acid portion". It was later learned (Rich, S., private communication) that this view was based on glass-slide experiments using spores of *Stemphylium sarcinaeforme* (Cav.) Wiltsh. as test organism, a spore suspension being added to the slide cavity after drying the initial solution or suspension of test substance. Germination was not inhibited by 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate, 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenol or crotonic acid alone, or by a mixture of the second and third, even at 0·1 per cent. If, however, the spores were added to a crotonic acid solution and this suspension incubated on slides, the *ED*50 was less than 0·003 per cent. These results were interpreted to mean that crotonic acid was easily lost from the ester and from a deposit on glass, and that fungitoxicity of 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate depended on crotonic acid being present at the time of interaction with spores.

In greenhouse investigations begun here in 1952 on the chemical control of apple powdery mildew, *Podosphaera leucotricha* (Ell. and Everh.) Salm., using M.III rootstocks in small pots, no promise of control was offered at 0·05 per cent by salts or simple esters of crotonic acid, or by a considerable range of esters of unsaturated acids or alcohols, or by various other compounds containing unsaturated bonds in the molecule. On the other hand, technical grade 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate or the free phenol, isolated from the crude ester, gave, at 0·025 per cent, prophylactic control of the disease equal to that given by 1 per cent lime-sulphur, indicating that the phenolic portion of the 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate molecule is mainly responsible for fungitoxic action, in this case at least.

Recently, a more satisfactory method of infection has made possible more critical tests. Ten pots, each with one barley seedling or one apple rootstock bearing 2–3 shoots, were used for each treatment. Chemicals in aqueous formulation (1 per cent acetone and 0·025 per cent 'Triton *X*-100') were applied by dipping ; spores were applied later by settling in a tower. Lesions were counted after 7 days for barley and 9 days for apple. It is hoped to publish full details of the methods elsewhere.

The results of two trials on barley and one on apple are given in Table 1, the 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate and the free phenol being used in equimolar ratios, and ammonium crotonate in equimolar, quadrimolar or quinquemolar ratio. In all three tests, the free phenol gave as good protection as the ester, whereas ammonium crotonate gave little or no protection against barley mildew, and only 60 per cent reduction of apple mildew at the quinquemolar rate.

Table 1

Treatment	Concentration (per cent)	Barley: Lesions per plant : First trial	Barley: Lesions per plant : Second trial	Apple: Lesions per leaf
Formulation control	—	40·9	92·5	6·87
DNOP	0·020	0·3	—	0·0
	0·016	—	0·2	—
DNOPC	0·025	0·2	—	0·0
	0·020	—	0·8	—
Ammonium crotonate	0·007	41·5	—	—
	0·028	—	115·2	—
	0·035	33·6	—	2·74

DNOP = the free phenol ; DNOPC = 2 : 4-dinitro-6-(1-methyl *n*-heptyl)phenyl crotonate.

Further greenhouse trials have shown that control of apple and barley mildews comparable to that given by 1 per cent lime-sulphur can be obtained under these conditions with the free phenol at 0·0025 and 0·007 per cent, respectively. Moreover, a large degree of control was achieved at 0·01 per cent with 2 : 4-dinitro-6-*n*-octylphenol on apple, and with 2 : 4-dinitro-6-*cyclo*octylphenol on barley ; all the octyl isomers caused scorching of barley leaves, and the *cyclo*-octyl compound was toxic to apple also. The 6-*n*-hexyl and 6-*n*-heptyl homologues were also effective on apple, but very toxic to barley ; the 6-*cyclo*hexyl homologue, dinex, was almost non-toxic to barley even at 0·05 per cent, but mildew control was poor. The 6-chloro homologue was very promising on barley, but very toxic to apple, at 0·02 per cent ; picric and picramic acids were safe at 0·015 per cent on barley but afforded little control of mildew.

It is well known that powdery mildews are largely unaffected by chemicals that are toxic to many other types of fungi. Thus the results obtained with 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate and its components on two powdery mildews, which were diametrically opposite to those reported by Rich and Horsfall for *S. sarcinaeforme*, might be peculiar to the Erysiphaceae. Results are therefore of interest from tests conducted with two well-known fruit pathogens, *Venturia inaequalis* (Cke) Wint., and *Botrytis cinerea* Pers. ex Fr., using a glass-slide spore-germination technique already described[2] that is basically similar to that used by Rich and Horsfall.

Table 2

Treatment	Concentration (per cent)	Inhibition of germination (per cent)	
		V. inaequalis	*B. cinerea*
DNOP, freed from ester	0·01	100	10·3
	0·001	33·5	1·5
	0·0001	4·6	0·0
DNOPC, freed from phenol	0·01	100	1·2
	0·001	19·2	0·0
	0·0001	14·6	0·0
DNOPC, crude	0·01	100	2·8
	0·001	31·1	0·0
	0·0001	0·0	0·0

DNOP = the free phenol; DNOPC = 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate.

Formulation was in 8 per cent acetone and 0·05 per cent sulphite lye, the spore suspension being placed on the dry deposit. The results obtained with both organisms, corrected to the formulation control by Abbott's formula, are given in Table 2, and leave little doubt that the activity of 2 : 4-dinitro-6-(1-methyl-*n*-heptyl)phenyl crotonate, crude or purified, is due almost entirely to the phenolic component, the ester probably being decomposed at some stage after deposition on glass, as it may well be on foliage.

We are indebted to our colleagues, Mr. R. P. Tew, for provision of 2 : 4-dinitro-6(1-methyl-*n*-heptyl)phenyl and several *n*-alkyl homologues, and Dr. M. H. Moore, for much help in developing methods and for recording the first series of trials, and to British Oxygen Research and Development, Ltd., for a gift of the *cyclo*-octyl homologue.

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Biosynthesis of Plant Glycosides from Uridine Diphosphate Glucose

The formation of glycosides and gentiobiosides after adding phenols or other substances to whole plant tissues has been observed by several workers[1-3]. Extracts of *Vicia faba* were reported by Miwa *et al.*[4] to form glucosides from vanillin, salicylaldehyde and hydroquinone. Tabone[5] prepared a partially purified enzyme from lentils which on addition of uridine diphosphate glucose and anthranilic acid formed a compound in which the carboxyl group of anthranilic acid was joined to a β-glucosyl residue.

The formation of phenol glycosides has been reported previously[6]: incubation of wheat-germ extracts with uridine diphosphate glucose and hydroquinone was found to lead to the appearance of a compound which appeared to be identical with arbutin (*p*-diphenol-β-glucoside) as judged by its mobility on paper before and after acid or enzymatic hydrolysis. Incubation of hydroquinone with other possible glucose donors, such as glucose-1-phosphate, sucrose, cellobiose or maltose gave negative results. Other phenols, such as saligenin (*o*-hydroxybenzyl alcohol), pyrocatechol (*o*-diphenol) and resorcinol, also reacted in the system to yield the corresponding β-glucosides, that is, salicin, pyrocatechol-and resorcinol-β-glucoside respectively.

In the course of studies on the formation of hydroquinone glucoside, it was observed that another substance besides arbutin was formed. As shown in Table 1, an unknown compound was found (R_F 0·08) in addition to hydroquinone (R_F 0·83) and arbutin (R_F 0·35) when the reaction mixture was chromatographed on paper.

In view of the lower mobility, it was considered likely that the compound with R_F 0·08 might have more than one glucose residue. Experiments carried out with arbutin instead of hydroquinone as substrate showed that the slowly moving compound (R_F 0·08) was formed more rapidly and in larger amounts. Up to 0·2 μmole was formed in 30 min. in the system mentioned in Table 1, with 2 μmoles of arbutin in place of 10 μmoles of hydroquinone.

For the identification of the new compound the reaction products were run on paper with butanol/pyridine/water (6 : 4 : 3) as solvent, thus obtaining a good separation from free glucose and from another unknown substance which remains near the origin with aqueous butanol. The new substance, after rechromatography and elution from the paper, gave an absorption curve in the ultra-violet very similar to that of arbutin. After acid hydrolysis in 1 *N* hydrochloric acid for 60 min. at 100° C. followed by paper chromatography, only glucose and hydroquinone were detected. Incubation with purified emulsin for 24 hr. gave glucose, arbutin and hydroquinone.

Estimation of phenol by the method of Folin and Ciocalteu[7] against an arbutin standard and of glucose by the phenol/sulphuric acid procedure[8] showed that the ratio glucose/phenol was about 2. The same results were obtained by estimating the glucose with an alkaline copper reagent[9] after complete hydrolysis with emulsin. By partial acid hydrolysis (10 min. in 1 *N* hydrochloric acid at 100°) followed by paper chromatography and development with alkaline silver[10] it was found that in addition to glucose a more slowly migrating sugar appeared. The latter was separated from parallel runs and compared with different disaccharides. Its behaviour proved to be identical with that of gentiobiose upon paper chromatography with several solvents (butanol/pyridine/water, 6 : 4 : 3; butanol/acetic acid/water, 4 : 1 : 5; and propanol/ethyl acetate/water, 7 : 1 : 2), and only glucose was formed on acid hydrolysis. Thus the results indicate that the compound is β-gentiobiosylhydroquinone. No mono- or di-glycosides were detectable in experiments in which the following substances were substituted for uridine diphosphate glucose: uridine diphosphate-acetyl glucosamine, guanosinediphosphatemannose, sucrose, glucose-1-

Table 1

Addition	Hours of incubation at 37° C.	R_F		
Uridine diphosphate glucose (1 μmole)	3	0·08	0·35	0·83
—	3	—	—	0·83
Arbutin (2 μmoles)	0	—	0·35	0·83
Arbutin (2 μmoles)	3	—	0·35	0·83

The system contained: 10 μmoles of hydroquinone, 50 μmoles of *tris* buffer *p*H 7·4 and 0·1 ml. of enzyme. Total volume 0·3 ml. The enzyme was prepared by extracting wheat germ with 3 volumes of 0·05 *M* phosphate buffer of *p*H 7, precipitating with ammonium sulphate between 0·2–0·5 saturation and dialysing. The deproteinized samples (ref. 9) were spotted on paper and run for 20 hr. with *n*-butanol saturated with water. Diazotized *p*-nitroaniline was used as developer (ref. 11).

phosphate, cellobiose, gentiobiose or maltose. Arbutin by itself was not hydrolysed or transglycosidated by the wheat-germ extracts, so that the mechanism of action is different from that described by Pridham[11], who reported the formation of β-gentiobiosyl-hydroquinone and glucose from arbutin with a plant β-glycosidase.

It thus appears that two transfer reactions from uridine diphosphate glucose are catalysed by the wheat-germ extracts: (1) the formation of the β-glucoside of hydroquinone (arbutin) and (2) the glycosylation of the glucose residue of the latter at the 6 position to yield gentiobiosyl-hydroquinone. It has not been established whether one or two enzymes are involved.

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Failure to induce Immunological Tolerance during Recovery from Irradiation

Neonatal animals and animals given large doses of whole-body X-irradiation are immunologically similar in two important respects: both are very poor producers of antibody, but both become satisfactory producers of antibody after several weeks, presuming that the X-irradiated animals survive. It is well established that during normal maturation animals go through a stage during which they may be rendered immunologically tolerant of certain antigens[1], and it seemed of considerable interest to determine whether, following severe X-ray damage, a similar stage occurred during which tolerance could be induced by appropriate antigenic stimulation. As X-ray damage is followed by rapid proliferation and differentiation of mesenchymal cells, be they the animal's own or bone-marrow cells grafted from a normal donor, it seemed possible that there might be a stage during which potential antibody-producing cells could be modified by contact with antigen and rendered immunologically tolerant.

Numerous workers, including Simonsen[2] and Nossal[3,4], have shown that the repeated injection of large amounts of foreign erythrocytes into embryos or neonates is followed by immunological tolerance. Accordingly, in the first series of experiments here reported, adult male *C3H* mice (bred by brother–sister matings for over forty generations) were exposed to 850 r. of whole-body irradiation, and 1–4 hr. later were given intravenous injections of isologous bone marrow. The bone marrow from six bones of one normal adult male donor was injected into each mouse. On the day following irradiation, and twice per week for four weeks during the recovery phase, the mice received intraperitoneal injections of 0·1 ml. of 20 per cent (packed cell volume) washed rat erythrocytes suspended in physiological saline. Normal adult *C3H* mice given a similar course of injections served as controls. One week after the last injection, the mice were bled, and the hæmagglutinin titre of the sera against rat cells determined. While the titre of one of the irradiated animals was much lower than those of the controls, it is clear from Table 1 that no immunological tolerance had resulted.

Table 1. Antibody Production in Lethally Irradiated Mice

Lethally irradiated bone marrow grafted mice (serum agglutinin titres)	Normal mice (serum agglutinin titres)
10,000	10,000
10,000	10,000
10,000	10,000
10,000	10,000
10,000	10,000
600	>10,000

Similarly, when adult mice were sublethally irradiated with 600 r., and injected with rat erythrocytes twice weekly for four weeks, all animals developed high titres of rat erythrocyte agglutinin. Next, the possibility that immature animals X-irradiated just after the end of the 'critical period'[2] for the induction of tolerance might be rendered tolerant by antigenic stimulation was explored. Day-old mice were given 500–700 r. of whole-body X-irradiation, and were afterwards injected twice weekly with 0·1 ml. of 20 per cent rat erythrocytes for four weeks. One week later, the agglutinin titre of their sera was determined. In three experiments out of four, all mice had high agglutinin titres. In the fourth experiment, similar in design to the other three, half the recipients had very low titres when compared with non-irradiated control mice given similar injections. However, even in this group the suppression of the immune response was temporary, and had almost disappeared when the mice were given two challenge injections of erythrocytes three months later.

Finally, attempts were made to save lethally irradiated adult mice with grafts of embryonic hæmopoietic tissue and to induce tolerance in this grafted tissue by antigenic stimulation. Attempts to use embryonic liver to save lethally irradiated animals were unsuccessful. Jacobson[5] has reported that about 30 per cent of lethally irradiated mice could be saved by injections of whole-embryo emulsion after irradiation. We were able to save about 20 per cent of our lethally irradiated animals by injection of 1·0 ml. of a mince prepared from 16–17 day-old mouse embryos. When these mice were injected with rat erythrocytes twice weekly for four weeks, the majority developed rat erythrocytes agglutinins. Most of the remainder developed high agglutinin titres when injected with further doses of rat erythrocytes three months later. Out of 15 animals examined, only one was still

immunologically tolerant 20 weeks after irradiation, and it died shortly thereafter.

The failure to induce immunological tolerance in these circumstances is of considerable theoretical interest. It has been shown that mice lethally irradiated and saved with homologous bone marrow are thereby rendered immunologically tolerant of a skin graft from an animal of the donor strain[6]. During the very period when such a state of mutual tolerance is being developed, some cells, be it the proliferating grafted cells or the recovering host cells, evidently retain the capacity to produce circulating antibody to a heterologous antigen.

We wish to express our thanks to Sir Macfarlane Burnet for his interest in this work, and to the staff of the Peter MacCallum Cancer Clinic, especially Miss Betty Rose, for performing the irradiations. This work was aided by a grant from the National Health and Medical Research Council, Canberra.

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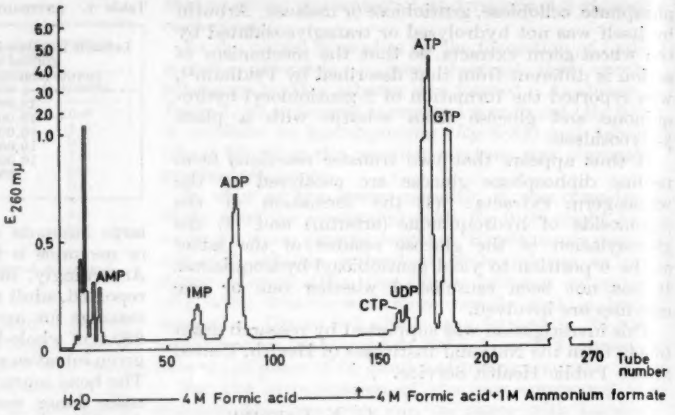

Fig. 1. Ion-exchange chromatogram of the acid-soluble nucleotides in the blood of metamorphosing salmon, taken during the pre-metamorphosis period (see text). 'Dowex 1' × 2 (200–400 mesh) column in the formate form, 0·9 cm. × 13 cm. Mixing volume, 250 ml.; flow-rate, 0·4 ml./min. Fraction volume, 5–4 ml. Key: AMP, adenosine monophosphate; IMP, inosine monophosphate; ADP, adenosine diphosphate; UDP, uridine diphosphate; ATP, adenosine triphosphate; CTP, cytidine triphosphate; GTP, guanosine triphosphate

Acid-Soluble Nucleotides from the Blood of Metamorphosing Salmon

In a search for possible precursors to the guanine that appears in large amounts in the skin of the salmon (*Salmo salar*) at the transformation from parr into smolt, blood samples from fishes in different stages of metamorphosis were collected and subjected to ion-exchange chromatography. The blood samples were obtained by cutting the tails of a number of fishes (as nearly equal in size as possible) and collecting the blood in a vessel cooled by a mixture of acetone and 'dry ice'. The frozen samples were extracted with 0·6 *N* and 0·3 *N* perchloric acid, neutralized by potassium hydroxide, and put on a 'Dowex 1' × 2 column in the formate form. The various fractions were eluted by the gradient elution technique of Hurlbert and his co-workers[1], as modified by Schmitz[2]. Extinction values of each fraction were read at 260 and 280 mμ in a Beckman spectrophotometer model *DU*. The various components were identified by their characteristic 260/280 mμ ratios[3], by their positions in the chromatogram, and by their ultra-violet absorption curves. For further analysis appropriate fractions from the peaks in the chromatogram were pooled, desalted by passing through a 'Dowex 50' column, evacuated to dryness at 20° C. and finally dissolved in a small volume of distilled water. Using the millimolar extinction coefficients given by Hurlbert and co-workers[1] the various compounds were estimated quantitatively. Base–ribose-phosphate ratios were based upon measurements of ultra-violet extinction values, analysis of total and acid-labile phosphate by the method of Berenblum and Chain[4], and analysis of ribose with the orcinol – hydrochloric acid method as modified by Hurlbert *et al.*[1].

It is apparent that with respect to nucleotide content of the blood, metamorphosis can be divided into three time-periods. The first, or pre-metamorphosis period, is dominated by a high guanosine triphosphate

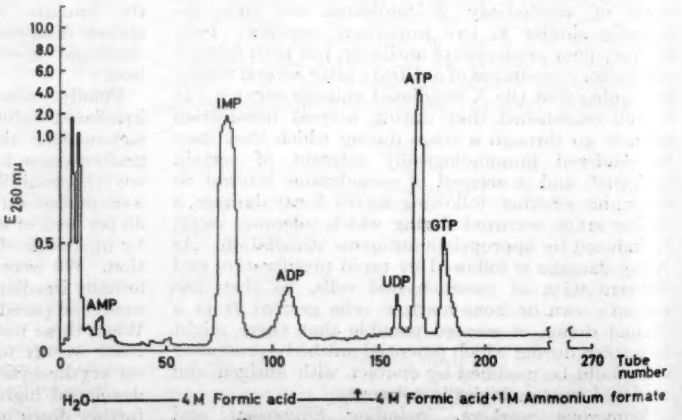

Fig. 2. Ion-exchange chromatogram of the acid-soluble nucleotides in the blood of metamorphosing salmon, taken during the metamorphosis period (see text). Conditions and key as for Fig. 1

and a low inosine monophosphate content (Fig. 1). During this period there is no pronounced deposition of guanine in the skin. The next period, the metamorphosis period, is characterized by a high inosine monophosphate content of the blood, a high rate of guanine deposition, and a reduced guanosine triphosphate content of the blood (Fig. 2). In the third or post-metamorphosis period the inosine monophosphate content of the blood has also been reduced to a low level so that, with respect to nucleotide content, the blood is quite comparable with that of a non-metamorphosing salmon.

A comparison with values for animal tissues given in the literature[5,6] indicates that guanosine triphosphate occurs in remarkably high concentrations in the blood of the salmon, especially during the pre-metamorphosis period, when it amounts to about 30 per cent of the adenosine triphosphate value. But also during non-metamorphosing periods the guanosine triphosphate content of the blood of salmon is high as compared with, for example, muscle tissues, which have been reported by Bergkvist and Deutsch[5] to contain guanosine triphosphate in amounts of about 1 per cent of that of adenosine triphosphate. The corresponding figure for the blood of salmon is about 10 per cent.

Full details of this investigation will be published elsewhere.

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Toxic Effects produced by Pyrimethamine in Chickens and their Antagonism by Folic Acid

PYRIMETHAMINE, a folic acid antagonist, has been shown to potentiate the activity of sulphadimidine and sulphaquinoxaline against cæcal coccidiosis in chickens (ref. 1 and Ball, S. J., private communication). During our investigation of this combination, the decreased growth-rate and anæmia observed in Rhode Island × Light Sussex chickens fed for 28 days on an all-mash diet containing 20 p.p.m. of pyrimethamine, appeared to be controlled by a dose of 10 mgm./kgm. folic acid. The mean weight gain over the experimental period is shown in Table 1.

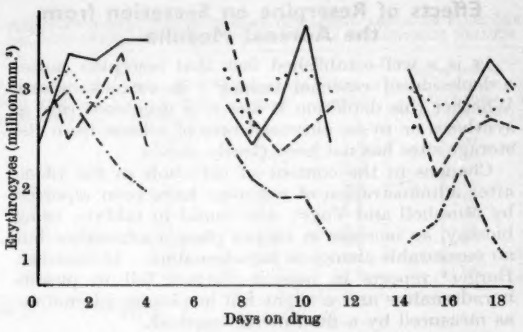

Fig. 1. ....., Control; —.—.—, pyrimethamine, 20 p.p.m.; ———, folic acid; – – – –, pyrimethamine 20 p.p.m. + folic acid

Daily erythrocyte counts were made in blood taken from the wing vein (Fig. 1). After 21 days the erythrocyte count, hæmatocrit and hæmoglobin concentration in the heart blood and the total liver iron content of each of the birds were measured (Table 1). Sections of liver, treated with potassium ferrocyanide, were examined for hæmosiderosis.

Pyrimethamine (20 p.p.m.) in the feed caused a significant depression of gain in weight ($P<0.03$) and a macrocytic, hyperchromic type of anæmia. These effects were not present in the chicks receiving folic acid injections in addition to the pyrimethamine. The folic acid injections alone produced no effect on gain in weight or on the blood measurements.

There was a significant increase ($P < 0.05$) in the total iron content of the livers of the chicks (Table 1) receiving pyrimethamine only, and hæmosiderosis was noted in liver sections treated with potassium ferrocyanide, from the birds in this group. These latter observations suggest that a hæmolytic process, in addition to any effects produced on erythropoesis, is involved in the production of anæmia, a finding previously reported by Zach[2], who detected free hæmoglobin in the serum of rats receiving pyrimethamine.

From this work it appears that the toxic effects of pyrimethamine were caused by a state of folic acid deficiency, as they were controlled by the administration of folic acid.

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Table 1. MEAN WEIGHT GAIN, MEAN CELL VOLUME AND MEAN CORPUSCULAR HÆMOGLOBIN CONCENTRATION IN CHICKENS AFTER 21 DAYS

Pyrimethamine in diet (p.p.m.)	Folic acid injections (i.p.) (dose × 2 weekly)	Mean weight gain (gm.) ± S.E.	Heart blood					Liver Mean total iron content (mgm. per cent) ± S.E.
			Red blood cell count (× 10⁶/mm.³)	Hæmatocrit (per cent)	Hæmoglobin (per cent)	M.C.V. (μ^3)	M.C.H. ($\mu\mu$gm.)	
0	—	241·2 ± 19·14	2·41	30	9·1	126	35	37·7 ± 2·2
	100 mgm./kgm.	227 ± 20·1	2·38	29	8·7	121	36	33·8 ± 3·5
20	—	145·0 ± 16·95	1·18	18	6·3	154	52	82·2 ± 14·8
	100 mgm./kgm.	233·0 ± 13·06	2·46	30	9·5	119	38	40·0 ± 5·0

Effects of Reserpine on Secretion from the Adrenal Medulla

It is a well-established fact that reserpine causes a depletion of catechol amines[1,2] in various organs. Whether this depletion is due to a decreased rate of synthesis or to an increased rate of release from the storage sites has not been clearly shown.

Changes in the content of catechols in the blood after administration of reserpine have been reported by Muscholl and Vogt[3], who found in rabbits, using biossay, an increase in venous plasma adrenaline but no measurable change in noradrenaline. In contrast, Burger[4] reports in man a distinct fall in plasma noradrenaline and a slight fall in plasma adrenaline, as measured by a fluorimetric method.

In the experiments reported here the purpose has been to determine whether reserpine causes secretion of medullary hormones into the adrenal venous blood.

To cats of both sexes, weighing 3–4 kgm. and anæsthetized with 'Nembutal' (Abbott), given intraperitoneally, 3 mgm./kgm. reserpine ('Serpasil', Ciba) was administered intravenously. Collections of adrenal vein blood were made at intervals using a special shunt technique (Schapiro and Stjärne, to be published). The adrenal vein plasma and the organ extracts were assayed biologically (cat's blood pressure and hen's rectal cæcum).

Reserpine was found to cause a transitory fall in blood pressure in every experiment except one, in which both vagi had been cut and the carotid sinus denervated bilaterally. In this case a gradual pressor effect was observed, lasting for 20 min. with a maximum value 40 mm. mercury above the resting level.

In every experiment reserpine caused a well-marked increase in the secretion-rate of both adrenaline and noradrenaline. The increase was already present in the first collection period 10–15 min. after reserpine was given; it reached its maximum value 1½–2 hr. later (Fig. 1). The effect on noradrenaline secretion was consistently greater than that on adrenaline, noradrenaline making up 75–90 per cent of the total catechols released. The amount of noradrenaline recovered in the adrenal vein blood in some experiments is so large that it suggests an increased rate of resynthesis, at least initially (Table 1).

The results of our experiments suggest that reserpine causes a relatively selective mobilization of noradrenaline. This is in accordance with the results reported by Eränkö and Hopsu[5]. These workers have shown by histochemical methods in rats that reserpine causes typical secretory changes almost exclusively in the parts of the adrenal medulla containing noradrenaline. The initially increased resynthesis-rate observed by us during the first 2–3 hr. after the administration of reserpine is of special interest in view of reports (refs. 6 and 7 and Bygdeman, S., and von Euler, U. S., personal communication) showing that direct electrical stimulation of the splanchnic nerve causes an acceleration of synthesis. However, the dose of reserpine used by us is known to cause an almost complete emptying of the adrenal medulla in 16–24 hr. Thus it seems clear that in the long run resynthesis cannot keep pace with secretion.

Other experiments of ours (in preparation) as well as by others[1,2,8] indicate that the effect of reserpine on the adrenal medulla is to a large extent dependent on the innervation of the gland being intact.

This investigation has been supported by a grant to one of us (L. S.) from Svenska Nationalföreningen mot Tuberkulos och andra Folksjukdomar.

Table 1. Adrenaline and Noradrenaline in the Adrenal Medulla after Experiment 10, as compared to the Recovery in the Adrenal Vein Plasma after Reserpine

The calculation of the output is based on the assumption that during each shunt period the secretion can be represented by the average of the collection period immediately before and after it

Weight of left adrenal gland, 295 mgm.	Adrenaline (μgm.)	Noradrenaline (μgm.)
Content of left adrenal after the experiment (*a*)	62	15
Recovery in adrenal vein blood after reserpine (*b*)	91	282
Total amount recovered (*a* + *b*)	153	297

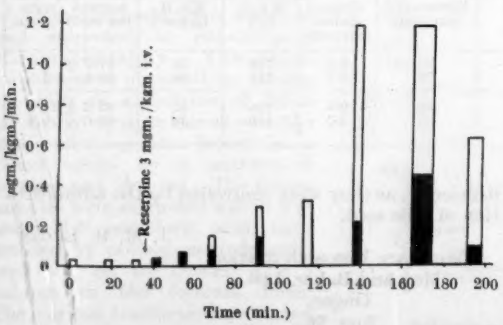

Fig. 1. Secretion of adrenaline and noradrenaline after the intravenous administration of 3 mgm./kgm. reserpine. White, noradrenaline; black, adrenaline

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Behaviour of 19-nor-Progesterone and 19-nor-Ethinyltestosterone in the Liver of the Guinea Pig.

The anticestrogenic properties of 9-α-fluoro-11-β-hydroxyprogesterone are superior to those of 11-β-hydroxyprogesterone[1]. The halogenated compound resists inactivation in the liver[2]. This resistance has been corroborated in a new set of experiments (Table 1, *A*, *B* and *C*), from which it is evident that a given amount absorbed from an intrasplenic pellet (*B*) is less active than when absorbed from a subcutaneous one (*A*). There is no doubt, however, as to resistance of the halogenated compound in the liver (compare *B* and *C* with I*b*). Thus greater activity, namely, enhanced antifibromatogenic, antihysterotrophic and antiluteinizing properties of the halogenated, as compared with the non-halogenated

Table 1. EXPERIMENTS ON EIGHTY-EIGHT CASTRATED GUINEA PIGS RECEIVING DURING THREE MONTHS ŒSTRADIOL ABSORBED FROM SUBCUTANEOUSLY IMPLANTED PELLETS, AND VARIOUS ANTIŒSTROGENIC STEROIDS ABSORBED FROM SUBCUTANEOUS OR INTRASPLENIC PELLETS

Group	Antiœstrogenic steroid	Administered	No. of animals	Œstradiol (μgm./day)	Antiœstrogenic steroid tested (μgm./day)	Fibrous tumoral effect (average)	Coefficient Q_{1-5}*	Uterine weight	No. of pellets and concentration of compound (per cent)
A	9α-F-11βOH-P	Subcutaneous	7	44	1	1·4	0	1·6	1 ; 20
B	9α-F-11βOH-P	Intrasplenic	9	56	1	1·7	0·11	1·4	1 ; 20
C	9α-F-11βOH-P	Intrasplenic	7	44	8	1·9	0·14	1·9	1 ; 40
Ia	Progesterone	Subcutaneous	10	48	9	1·5	0	3·3	½ ; 40
Ib	Progesterone	Intrasplenic	8	53	12	7·8	2·5	4·2	½ ; 40
IIa	19-nor-P	Subcutaneous	9	51	1·6	1·4	0	3·1	½ ; 20
IIb	19-nor-P	Intrasplenic	8	48	1·1	5·7	1·7	5·9	½ ; 20
IIc	19-nor-P	Intrasplenic	6	45	9	3·0	0·7	5·6	½ ; 40
IIIa	19-nor-ET	Subcutaneous	14†	50	80	2·0	0·3	2·6	½–1 ; 100
IIIb	19-nor-ET	Intrasplenic	10	46	65	2·0	0·2	3·8	½ ; 100

* Taken for comparison from ref. 5*a*. † See ref. 1*b*.

compound, could be explained, in part at least, by a different behaviour of the two compounds in the liver.

The question now arises whether the same is true for 19-nor compounds. The antiœstrogenic activity of 19-nor-progesterone (19-nor-P) is (like its progestational potency[3]) much greater than that of progesterone[4]. It is the same with 19-nor-ethinyltestosterone (19-nor-ET)[5], and 19-nor derivatives of testosterone compared with the natural androstenes[6].

We have now studied the antifibromatogenic action of progesterone and 19-nor-progesterone absorbed[7] from pellets implanted in the spleen. The results show that both substances are undoubtedly inactivated in the liver (Table 1; for details see Fig. 1). With intrasplenic pellets of either progesterone or 19-nor-progesterone (*Ib* and *IIb*) the fibrous tumoral effect is as great as in animals receiving œstrogen only; similar quantities absorbed from subcutaneous pellets (*Ia* and *IIa*) produce a very notable antifibromatogenic effect. The same holds for the comparative antihysterotrophic effects with subcutaneous and intrasplenic pellets.

One might argue that in *IIb*, with intrasplenic pellets of 19-nor-progesterone, the average quantity absorbed per day was somewhat smaller than in *IIa* with subcutaneous pellets. But this argument is invalidated by the fact that, even with 9 μgm./day of 19-nor-progesterone absorbed from intrasplenic pellets (*IIc*), no definite antifibromatogenic effect is obtained which would be comparable to that obtained with a quantity five or six times smaller when absorbed from subcutaneous pellets (*IIa*). Indeed, the fibrous tumoral effect in *IIc* was not so great as in *Ib* and *IIb*. But this insignificant antitumorigenic effect was evidently due to very small quantities of the highly active 19-nor-progesterone which escape intrahepatic inactivation; the same happens even with the less-active progesterone when absorbed from intrasplenic pellets[7].

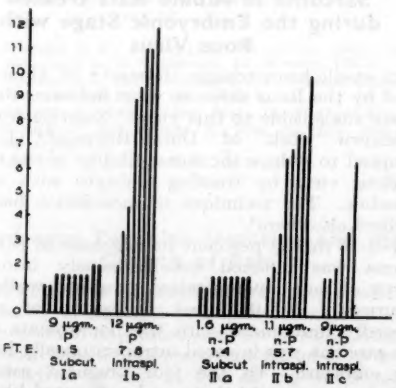

Fig. 1. Fibrous tumoral effect (FTE) in arbitrary units in guinea pigs with subcutaneously implanted pellets of œstradiol. Thick lines, animals with an additional subcutaneous pellet of progesterone or 19-nor-progesterone. Thin lines, animals with an additional intrasplenic pellet of progesterone or 19-nor-progesterone. When absorbed from the spleen both progesterone and 19-nor-progesterone lose their antifibromatogenic activity

Experiments with 19-nor-ethinyltestosterone are also of interest. It is known that progestational action can be obtained with ethinyltestosterone when given by mouth; this presupposes good resistance in the liver. The antifibromatogenic potency of ethinyltestosterone is inferior to that of progesterone and reaches only that of testosterone[8]; but 19-nor-ethinyltestosterone is several times as potent as ethinyltestosterone[1c, 5b]. How will 19-nor-ethinyltestosterone behave when absorbed from an intrasplenic pellet? A comparison between *IIIa* and *IIIb* (Table 1) shows that there is no difference in the results obtained with subcutaneous and intrasplenic pellets of 19-nor-ethinyltestosterone. Thus the latter resists inactivation in the liver. In other words, the 19-nor configuration is of no consequence with regard to resistance in the liver (19-nor-ethinyltestosterone), and neither is it of any consequence as to non-resistance (19-nor-progesterone).

Thanks are due to Messrs. Syntex, Mexico, for progesterone and 19-nor-progesterone; to Prof. Carl Djerassi, Waine University, Detroit, for 19-nor-ethinyltestosterone.

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Conditions which eliminate Inflammation to Homografts in Rabbits

The stimulus for production of a sterile cellular infiltrate, principally lymphocytic, in and about a homograft remains obscure. Methods whereby this inflammatory reaction may be eliminated are worthy of consideration with the view of successful homografting between members of genetically impure strains.

Previous studies using musculofascial transplants of erector spinæ of rabbits permitted accurate distinctions to be made by ordinary histological methods between autografts and homografts[1]. Microscopic examination two weeks after implantation showed that both types of grafts underwent similar sequences of degeneration, resorption and organization, but in the homograft inflammation was superimposed upon the repairative matrix of the musculofascial zone. Angiitis involving the newly formed channels was a frequent feature of the inflammatory reaction.

Further experiments have shown that the classical inflammatory aspects of host–homograft interactions may be eliminated by several conditions. One condition was by reduction of 'viability' of tissues of the musculofascial graft by exposure to extremes of heat, cold or X-irradiation prior to implantation[2,3]. Both types of grafts so treated elicited a sluggish fibro-collagenous response by the host. Grafts studied following less extreme exposure to temperature and X-irradiation showed that the degree of admixture of proliferating cells of the graft with those of the host seemed to determine the magnitude of the inflammatory reaction in homografts.

A second condition for the elimination of inflammation in homografts required grafting between parabionts in the post-parabiotic period. Rabbits surgically united by the ears developed a cross-circulation lasting between 7 and 13 days after anastomosis[4]. The cessation of the cross-circulation seemed to be related to the development of inflammation at the surgical plane of anastomosis between the animals. Joining rabbit parabionts a second time failed to reproduce sequences of healing noted at primary junctions. This was in accord with the "second set rejection phenomenon"[5]. Microscopic study of cross-homografts between parabiotic partners following one and two periods of parabiosis showed two types of tissue reaction equally distributed between the two groups of parabionts[6]. The first type consisted of a fibro-collagenous encapsulation of the graft by the host in the absence of vascular penetration. Inflammation did not develop. The second type of post-parabiotic modification was similar to the first, with the exception that a peculiar angiomatous vascular plexus of capillaries arising from the host grew beneath the fascia of the homograft. Inflammation was again absent.

The third condition required cross-transfusion. Since a transient cross-circulation was a conspicuous feature of the primary healing between parabionts, cross-transfusions of whole blood, controlled in quantity, were done between pairs of rabbits[7]. This eliminated all factors involved in parabiosis except exchange of blood. The microscopic study of cross-homografts following cross-transfusions showed a vascularizing stromal penetration identical to the second type of host–homograft interaction following parabiosis. Inflammation was absent.

A fourth condition required for elimination of inflammation in homografts was the pregnant state. Gravid rabbits (13–15 days of gestation) were cross-grafted with males and non-pregnant females of the same species[8]. Autografts were also implanted. Each pregnant host reacted in the same way to autografts and homografts. Both types of grafts showed the usual sequences of degeneration, absorption and organization in the absence of inflammation characteristic of host–autograft reactions. It appeared that pregnancy lessened the capacity of the animal to react against grafts of normal homologous tissues.

These observations have indicated that investigation of the means by which the inflammatory aspects of host–homograft interactions are eliminated may offer clues to the solution of the problem of successful homografting.

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Sarcoma in Albino Rats treated during the Embryonic Stage with Rous Virus

The cystic-hæmorrhagic disease[1,2] of albino rats caused by the Rous sarcoma virus indicates that the rats are susceptible to this virus. Starting from the well-known work of Duran-Reynals[3,4] I have attempted to reduce the susceptibility of the rats to the Rous virus by treating embryos with specific antibodies. The technique of inoculation has been described elsewhere[5].

0·1–0·15 ml. 50 per cent homogenate of the Rous sarcoma was injected subcutaneously into each embryo of four laparotomized pregnant white rats. Concurrently 0·2–0·25 ml. antiserum of rabbits repeatedly immunized with the homogenate of the Rous sarcoma was injected intraperitoneally into the same embryos. Of the four pregnant rats, two aborted, one gave birth to and suffocated its litter, and only one bore successfully five rats, of which two were suffocated.

In two of the three surviving rats small, very slowly growing cysts developed one month after the

inoculation, but these regressed in course of time; 6 and 7 months thereafter sarcomata developed in these two rats. In one of them sarcoma appeared on the dorsal side of the neck, precisely at the site of primary infection with the Rous virus. The tumour attained the size of an apricot; histologically it was a sarcoma with a significant polymorphism resembling the Rous sarcoma. In the tissue spindle-like cells predominated, along with rounded cells and much mucopolysaccharide. In the second rat a 2-cm. sarcoma with spindle-like cells developed on the cheek.

The sarcoma was minced with scissors and sub-cultured in rats of various ages. It grew well in new-born rats, and within 20–25 days reached a large size, causing death in some animals. In young rats (50–60 gm.) growth of the tumour proceeded more slowly; it attained a large size in some of them. The weight of the tumour in such cases reached the weight of the rat itself, although in some individuals growth was poor, being followed by regression. In adult rats weighing 120–150 gm. the tumour reached the size of a bean and was then resorbed. In new-born and young rats the tumour grew on the second and third passages as well. Here the tumours were characterized histologically by appreciable homogeneity, being composed exclusively of spindle-shaped cells containing less mucopolysaccharide and being more solid than the initial tumour. The inoculation of minced rat sarcomata to chickens was unsuccessful. It is possible that the Rous virus is present in the rat tumours in the masked form.

It might seem that the inhibition of the pathogenic effect of the Rous virus by antiserum led to the development of sarcomata instead of the typical cystic-hæmorrhagic disease in rats infected during the embryonic period. Yet in one of the rats inoculated with the Rous virus during the prenatal period, without additional treatment with antiserum, a slowly growing cyst developed, which, seven months afterwards, was replaced by a huge sarcoma.

These experiments were carried out on rats of a stock free from spontaneous malignant tumours.

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Hydrogen Peroxide Ingestion and the Growth of Rats

Several recent communications have dealt with the capacity of ingested hydrogen peroxide to affect the regression of implanted tumours in rats. Holman[1] has claimed that a 0·45 per cent solution of hydrogen peroxide given to rats in lieu of tap-water caused regression of certain tumours; the opposite conclusion has been stated by Green and Westrop[2] and by Ghadially and Wiseman[3]. Accordingly, it seemed important to determine the effect of hydrogen peroxide on normal rats.

In one experiment, two groups of weanling male rats of the Osborne-Mendel strain developed at this Station were given a commercial dog food meal, and either tap-water or 0·45 per cent hydrogen peroxide *ad libitum* for a three-week period. During the test period, the animals on tap-water consumed an average of 544 ml. each, whereas those on peroxide averaged only 282 ml. each. The decreased amount of liquid intake was reflected in the total body-weight; 156 gm. for those on tap-water against 108 gm. for those on peroxide. No differences in the fresh weight of the testes, kidneys or spleen of the two groups were found.

In order to equalize any effects of limited intake of liquid, another group of male weanling rats was offered 0·45 per cent hydrogen peroxide in lieu of tap-water for a three-week period. Daily consumption was recorded, and a comparable group of male weanlings was given an amount of tap-water equal to the liquid consumed by the animals on peroxide. This regimen was also continued for a three-week period. It was observed that the group of rats on tap-water were continually seeking water, whereas those on peroxide did not act in a similar manner. The average body-weight was 116 gm. for those on peroxide and 104 gm. for those on tap-water. An attempt was made to see if ingestion of peroxide affected the fresh weight of some of the internal organs. Calculated in terms of percentage of body-weight, no important differences were found in the testes, kidneys, spleen or heart. The dry weights of these same tissues, calculated as percentage of body-weight, also failed to show differences.

Three weanling females were placed on a 0·45 per cent hydrogen peroxide regimen and maintained on it for five months. They were then given tap-water instead and were mated with normal males. Normal litters were produced. Six male litter mates were divided into two equal groups: one received peroxide while the other received tap-water. The animals were maintained on their respective regimens for nine months. The only noticeable effect was a difference in body-weight; an average of 521 gm. for those on tap-water against 411 gm. for those on peroxide. Three older males with an average weight of 600 gm. were given 0·45 per cent hydrogen peroxide for six weeks. At that time their average weight had fallen to 511 gm. They were then given tap-water and within two weeks had regained the lost weight.

Weanling rats offered the hydrogen peroxide *ad libitum* failed to gain weight normally. Although it had previously been shown that larger rats fed peroxide failed to gain weight normally[3], this phenomenon has not previously been noted for weanlings. Ghadially and Wiseman[3] attributed the loss of weight to diminished food intake; but, as noted above, this result may also be caused by a diminished liquid intake. Furthermore, long-term feeding of peroxide did not appear to affect reproduction in female rats.

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Role of Hypersensitivity in Experimental Staphylococcal Infection

It was shown previously[1] that a mild staphylococcal infection in rabbits can produce a state of both skin and systemic delayed hypersensitivity with some signs of immunity. Antitoxin formation, increased bactericidal activity of leucocytes and increased clearing of injected staphylococci from the blood and organs was found. Yet after a challenge with intravenous staphylococcal infection these rabbits died more rapidly and in larger numbers than normal controls. It has been also reported[2] that after production of hypersensitivity of the delayed type in guinea pigs using immunization with staphylococcal vaccine in Freund-type adjuvant, more numerous and larger abscesses are formed during the following infection; this conclusion has been given without detailed experimental results. In the experiments presented here an attempt was made to transfer to normal recipients this state of lowered resistance to staphylococcal re-infection passively, using cells of hypersensitive donors.

The desired state of hypersensitivity was produced in chinchilla rabbits by repeated intradermal and intravenous infections with small doses of staphylococci. Animals were selected after some weeks of treatment according to the intensity of skin reactions to diluted staphylococcal toxoid and vaccine given intradermally; in addition, α-antitoxin and agglutinin blood titres were determined. Spleen cells or peritoneal exudate cells (saline, 4 hr.) were transferred intraperitoneally to normal recipient rabbits; 200–300 million living cells were used. The exudate consisted of 10–30 per cent lymphocytes, 70–90 per cent polymorphonuclears and 5–10 per cent macrophages.

Normal rabbits with negative skin tests and without ascertainable antibodies were used as recipients and control donors. On the day following transfer the recipients were tested with staphylococcal toxoid and vaccine and reactions were recorded after ½, 2, 6, 24 and 48 hr. Following the last reading the animals were infected intravenously with 20 million micro-organisms of a virulent staphylococcal strain. Bacteriæmia was studied during infection and in some experiments the number of micro-organisms in different organs was also determined. Values of bacteriæmia for the last 24 hr. before death are not given.

As expected[3], transfer of cells resulted in skin hypersensitivity of the delayed type in the recipients. The results of staphylococcal infection in the experimental and control groups of rabbits are summarized in Table 1. It is evident that increased susceptibility to staphylococcal infection can be transferred with living cells from hypersensitive animals, while killed cells (65° C. for 30 min.) and cells from normal rabbits are without effect.

Table 1. Results of Staphylococcal Infection in Different Experimental Groups

	No. of rabbits	Deaths	Survivals	Deaths (per cent)
Hypersensitive rabbits	21	17	4	81
Recipients of hypersensitive cells	38	27	11	71
Recipients of killed hypersensitive cells	19	5	14	26
Recipients of normal cells	12	3	9	25
Normal rabbits	24	5	19	21

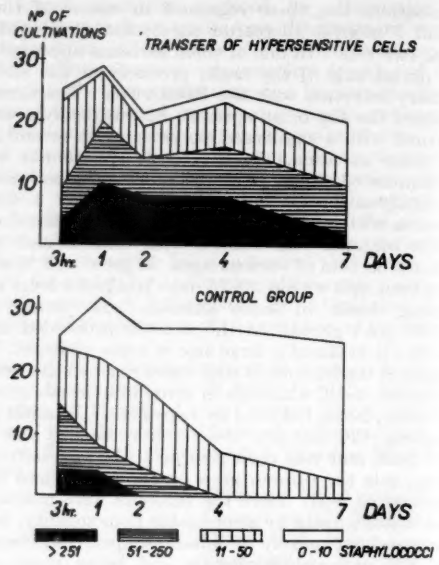

Fig. 1. Numbers of staphylococci cultivated from 1 cm.³ of blood during intravenous infection in rabbits passively sensitized with cells and in control rabbits

The bacteriæmia in rabbits previously sensitized with cells of hypersensitive rabbits remains high in the course of infection, while the bacteriæmia in control groups (normal rabbits, rabbits receiving normal cells or killed hypersensitive cells) declines progressively (Fig. 1). More micro-organisms are also found in organs. Cultivation from animals killed 48 hr. after infection gave the following average values per 100 mgm. organ-weight: in rabbits passively sensitized with cells—liver, 147; spleen, 156; lungs, 139; in control rabbits—liver, 3; spleen, 3·5; lungs, 4·5 micro-organisms.

The above results show that the state of increased susceptibility to staphylococcal infection can be transferred to normal recipient rabbits by means of living cells together with the delayed hypersensitivity to staphylococcal antigens. There is no direct evidence that there is a causal relationship between these two phenomena. There is no negative evidence, however, and no other reasonable interpretation can be given. It seems probable that the influence of hypersensitivity on the course of staphylococcal infection is due to changes (injury of cells, inflammation, etc.) that occur in tissues of sensitized animals after contact with the antigens of the infecting micro-organism; these changes may provide better conditions for the development of staphylococcal infection.

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Plasma Cells and Tumour Growth

GROWTH and regression of a tumour in experimental animals are known to be accompanied by various changes in the organs of the host, especially in the lymph nodes and spleen. Although there is a close association between immunity to a transplantable tumour and presence of local cellular infiltrations of, say, lymphocytes and plasma cells, there has been a wide diversity of opinion as to the specific cell or cells involved.

It is generally agreed that homografts of normal and tumour tissues are destroyed by a 'specific immune' reaction, but this still lacks the confirmation of direct demonstration of the presence of any antibody. Recent work has shown that plasma cells are involved in the production of antibody against bacterial, viral and other foreign protein antigens[1]. Several workers have also observed plasma-cell development in the host, following tumour[2] and normal tissue homografts[3].

I have approached the problem from a different angle, namely, by demonstrating plasma – cellular reaction in the tissues of the host, which may be considered as a pointer to the immunological changes taking place. A detailed histological and cytological study was made in rats to observe the local and remote reactions in the host, following transplanted and induced tumours, during the stage of progressive growth and regression, with special reference to the plasma-cell equipment.

Tuck male albino rats were employed throughout. Transplantable *Rd*/3 rat sarcoma (originally induced by 1 : 2 : 5 : 6-dibenzanthracene) and Walker carcinoma were used. Tumours were implanted subcutaneously into the right flank. Induced tumours were produced by subcutaneous injection of 1 : 2 : 5 : 6-dibenzanthracene in arachis oil. Tumour (*Rd*/3 and Walker) inhibition and regression were induced by intraperitoneal injection of 1 : 2 : 5 : 6-dibenzanthracene (2 mgm./100 gm. of body-weight) suspended in 0·2 per cent 'Teepol'. Animals were killed at different stages of tumour growth, inhibition and regression. Histological sections and smear preparations were made from these tumours and different organs, and stained with hæmatoxylin and eosin and Unna-Pappenheim (methyl-green and pyronin). The amount of plasma cells was estimated from these preparations.

In the normal rats, the lymph nodes, specially the axillary and para-aortic (lumbar) and the spleen contain very few plasma cells, mostly mature in type, in the medulla and red-pulp respectively. The main cellular constituents are the lymphocytes.

During the progressive growth of the transplanted tumour (*Rd*/3 and Walker), the draining lymph nodes, namely, the right axillary and para-aortic and the spleen are increased in weight. Some of these enlarged lymph nodes show hæmo-lymph node formation. Histologically, in the lymph node, the medulla is increased in size, replacing the cortical lymphoid tissue, and the sinuses are dilated. The broad medullary cords are crowded with proliferated reticulum cells and plasma cells (immature and mature), accompanied by diminution of lymphocytes. Russell-body cells are also found. Mitoses are frequent. No increase of plasma cells is seen in the cortex. In the hæmo-lymph nodes, large numbers of erythrocytes are found in the sinuses and many free macrophages show erythro-phagocytosis. In the spleen, the red pulp is highly cellular and shows proliferation of reticulum cells and increased number of immature and mature plasma cells, specially around the trabeculæ. The Malpighian follicles are not much affected and no increase of plasma cells are found. Transitions from reticulum cells to mature plasma cells are seen.

There is a significantly constant relation between the amount of plasma-cell response, weight of these organs and of the tumour. No definite relation between plasma-cell increase, hæmo-lymph node and metastasis formation is found. Moreover, the lymph nodes having secondary metastases show a marked diminution of plasma-cell reaction. A similar but less marked change is observed with tumours induced by dibenzanthracene.

The local reaction of the host around the tumour during its progressive growth is slight and the cellular infiltration is scanty, consisting of lymphocytes, macrophages, plasma cells and a few polymorphonuclear neutrophils, embedded in a connective tissue. Experimentally induced tumour inhibition and regression are regularly associated with an increased local reaction of the host around the tumour, consisting of accumulation of large numbers of plasma cells, without any appreciable alteration of the lymphocytic infiltration. This local plasma-cell accumulation is more numerous about the nodules of viable tumour cells, and in a few instances appeared to have invaded them, resulting in their degeneration and disappearance. When the tumour cells are no longer present, the local reaction subsides and the plasma-cell accumulation diminishes.

Following induced regression of the transplanted tumour, the animal becomes resistant to a subsequent challenge with the same tumour at a different site. Presence of living tumour cells is essential for this plasma-cellular response. Heat-killed tumour graft, which is no longer capable of stimulating this response, fails to render the host resistant to a subsequent inoculation with living tumour cells. Such a phenomenon is strongly suggestive of the presence of a circulating antibody.

These findings suggest that the increased response of plasma cells is the morphological manifestation of a systemic immune reaction to circulating antigen(s), which leave the graft, and reach the regional lymph nodes and spleen, where they excite this reaction, like any other antigens, and that plasma cells are involved in the production of antibodies. Other elements do not appear to have the same significance. Attempts to identify the antigenic substance in the tumour have so far been inconclusive.

Recent study of the nucleic acid content also supports the participation of draining lymph nodes in the formation of antibody against the transplanted tumour, and ribonucleic acid in these organs has been found to be increased, suggesting synthesis of protein[4]. Such enlarged lymph nodes have also been shown to take part in the immunological response conferring passive tumour transplantation immunity in secondary hosts[1,5]. Using the Schultz–Dale technique, it has been demonstrated that the presence of antibody in the host is the basic mechanism involved in this passive tumour transplantation immunity[1]. Further, the growth of the tumour cells is inhibited by treating them *in vitro* with excess of splenic and lymph-nodal cells from tumour-bearing animals. The only histologically demonstrable change in these organs taking part in the immunological phenomenon is the increased accumulation of plasma cells.

Cortisone, which abrogates the resistance to homo- and heterologous tumour grafts, inhibits this plasma-cell response in these organs. But once the immune reaction is established, cortisone fails to interfere with it, in spite of damage to the lymphocytes. This shows that cortisone strongly depresses antibody formation to antigens of the transplanted tumour tissue, by inhibiting plasma-cell development. These findings further show a constant relation between the plasma-cellular reaction and tumour resistance, which cannot be explained in terms of lymphocytes.

The conclusion which can be drawn from this study is that during reaction to bacterial and other foreign protein antigens, tumour and normal tissue-grafts, the plasma-cellular response may be considered as a pointer to the immunological change taking place. Judged by the plasma-cellular reaction, transplantation immunity to tumour and normal tissues conforms with the immune state generated by bacterial and other foreign protein antigens.

This work was carried out in the Cancer Research Unit, University of Sheffield, and I am indebted to Prof. H. N. Green for his interest and helpful discussions.

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Resistance to Flow in Vascular Beds

Dr. S. D. Carlill[1] has attacked the standard concept of resistance to flow (R) as the ratio of the driving force (the pressure drop P across the bed) to the flow F, and advocates that the 'dynamic resistance', that is, the differential dP/dF be substituted. His argument seems to assume what he is trying to prove.

Derived measures, or indices, depend for their usefulness on concepts that may underlie them. The standard measure of electrical resistance, in ohms, is used because we know that the applied potential difference plays a primary part in determining the current. Use of the ratio of voltage drop to current then allows us to remove the influence of this primary factor at the outset, and to concentrate on the other factors that determine the flow in a particular conductor. These factors are the specific conductivity of the material of the conductor, and its 'geometrical factor', that is, length over cross-sectional area.

The usefulness of the ohm is in no way dependent upon linearity between applied voltage and current. In modern electronics, perhaps the majority of the circuit components are non-linear (do not obey Ohm's law), yet we still use the ohmic resistance. We recognize, however, that the resistance of these components is not independent of the applied voltage, or of the current flowing. After all, Ohm's law itself has to make the condition that the resistance of a given conductor is constant, independent of the applied voltage, only if the temperature is kept constant (and actually the temperature must depend on the current flowing). By using the ratio of potential drop to current, that is, the ohmic resistance, we can study how the ratio depends upon other factors, including the voltage or current in non-linear cases.

With 'Newtonian' fluids flowing in cylindrical non-distensible tubes, Poiseuille's law applies. This is best written:

$$F = P \times \left(\frac{\pi}{8}\right) \times \left(\frac{1}{\eta}\right) \times \left(\frac{r^4}{l}\right) \quad (1)$$

$$= P \times (N) \times (V) \times (G) \quad (2)$$

where F is the flow, P the drop in pressure, (N) is the 'numerical factor', occurring in the integration of Hagen's theoretical treatment, (V) is the 'viscosity factor', and (G) is the 'geometrical factor' (r = radius, l = length of tube). On the standard definition, the resistance R is given by:

$$R = \frac{P}{F} = \frac{1}{(N) \times (V) \times (G)} \quad (3)$$

In the case cited, R is independent of P and of F.

When the flow-pressure curves are non-linear, as they are with blood flowing in vascular beds[2], we can legitimately consider that equation (3) still applies under any given condition of pressure and flow, but either the viscosity factor (V) or the geometric factor (G) is not constant but depends upon the pressure and the flow. If the vessels are distensible, their 'geometrical factor' (G) alters with the 'transmural pressure' of each of the vessels. If the fluid is non-Newtonian, having an 'anomalous viscosity', the viscosity factor (V) will depend on the rate of flow. Resistance of a vascular bed, therefore, depends on the pressure (not primarily upon the driving pressure, but on the 'transmural pressure'—for example, a rise of venous pressure greatly affects the resistance even if the driving pressure is kept constant[3]). The curves of resistance versus pressure are much as shown in Dr. Carlill's Fig. 1, and this has been pointed out many times by us and by others[1].

The point is that, in spite of this consideration, the resistance to flow, as the ratio of P/F, still tells us what the product of geometrical factor (G) and the viscosity factor (V) is for that set of conditions of pressure and flow. If, as fortunately it turns out to be, the viscosity factor has not changed appreciably[4], the change in the geometrical factor can be deduced from the change of resistance. If the resistance has increased, the vessels have become 'narrower'; if it has decreased the vessels have 'widened'. This is a big step in clarification, even though the question remains as to why the calibre of the vessels has changed. Was it because of a change in transmural pressure, or was it due to an 'active vasoconstriction' or 'vasodilation' (that is, due to contraction of the smooth muscle of the wall)? Often this question can be decided, in other cases not. For example, if the resistance has increased but the

pressures has not changed or has risen, this must have been active vasoconstriction, for the distensible vessels would passively decrease in size only if pressures fell. Thus the use of 'resistance to flow' greatly clarifies such problems.

Let us now consider Dr. Carlill's substitute for the conventional 'resistance', the 'dynamic resistance' dP/dF, derived from the slope of the flow-pressure curve. The 'instantaneous resistance' or its reciprocal, the 'transconductance', is, of course, familiar in electronics, where the slope of the characteristic for a given set of operating voltages, etc., is used in calculating amplification factors and the like. There will be a set of problems in hæmodynamics where the analogous 'dynamic resistance' is useful. These are those where the rate of change of flow in a vascular bed with change of blood pressure is relevant, for example, problems of control of circulation and its homœostasis. In our laboratory we have recognized this, as in the work of Girling[5], which points out how the level of blood pressure can greatly modify the effectiveness of the sympathetic activity.

Can the 'dynamic resistance' give us information, in any simple manner, as to what is happening to the calibre of the vessels? Differentiating equation (2) to derive the 'dynamic resistance' R':

$$\frac{1}{R'} = \frac{dF}{dP} = N\left[V.G + P.V.\frac{dG}{dP} + P.G.\frac{dV}{dP}\right] \quad (4)$$

If there were only the first term in the brackets we could associate changes in resistance with changes in the geometrical factor of the viscosity factor or both, but in non-linear cases the second and third terms may completely dominate the whole expression. A striking example where the substitution of the slope for the conventional resistance would lead to a paradox is at pressures close to the 'critical closing pressure' in vascular beds under considerable vasomotor tone. In this case the flow–pressure curve is markedly concave towards the pressure axis, and the slope becomes very steep as the point of zero flow is approached. One would be forced to say that the 'resistance' (that is, the 'slope' or 'dynamic' resistance) had become very low, for a very small change in pressure produces a large change in flow. Yet at the point where this 'dynamic resistance' is decreasing to a low value, the vessels are actually closing down. Clearly, no useful concept of the connexion between this 'dynamic resistance' and the size of the lumen of the vessels is possible. By all means let us use the 'slope' of the flow-pressure curves in proper context, but we must not substitute this 'dynamic resistance' for the standard 'Ohmologous' resistance of standard hæmodynamics. If we do, we are likely to make confusion worse confounded.

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Production of Mutants of Tobacco Mosaic Virus by Chemical Alteration of its Ribonucleic Acid *in vitro*

WHILE many agents are known to act as mutagens on the living cell, there have been no convincing reports that the genetic character of isolated particles, such as viruses or transforming principles, have been changed *in vitro*. Recent results with tobacco mosaic virus help to overcome this difficulty. The infective unit of the virus is its ribonucleic acid component, which can be isolated in active form[1]. It is made up of 6,000 nucleotides that probably form a single chain[2].

Recently, Schuster and Schramm[3] have used nitrous acid to convert adenine, guanine and cytosine into hypoxanthine, xanthine and uracil, respectively, while the ribonucleic acid strand remains intact. It was shown that the alteration of any one of about 3,000 nucleotides is lethal. Possibly, changes of other bases are mutagenic.

Table 1. MUTAGENIC EFFECT OF NITROUS ACID ON RIBONUCLEIC ACID. 2 vol. of 0·19 per cent ribonucleic acid extracted from tobacco mosaic virus *vulgare* by phenol (ref. 1) were mixed with 1 vol. 4 *M* sodium nitrite and 1 vol. 1 *M* acetate *p*H 4·8 at 22° C. After time *t*, the ribonucleic acid is diluted to 19 μgm./ml. with *M*/15 phosphate, and assayed. Control dilutions of untreated ribonucleic acid contain an equivalent amount of nitrite. Time τ (equation 1) is 18·5 min. Total infections are given as numbers of lesions (per leaf) on Xanthi, and as the sum of chlorotic and necrotic lesions on Java; mutant infections as numbers of necrotic lesions per leaf on Java

t (min.)	*t*/τ	Total infections		Mutant infections	Mutant infections (per cent)
		Xanthi	Java	Java	Java
1	0·05	72·8	183	1·4	0·8
4	0·22	72·4	130	2·5	1·9
8	0·43	89·8	188	4·5	2·4
16	0·86	59·3	97	5·4	5·6
32	1·73	36·1	63	6·6	10·5
64	3·46	10·4	21	2·1	9·8
96	5·2	2·7	3·5	0·5	15·5
Untreated controls, μgm./ml. ribonucleic acid					
19		155	138	0·3	0·2
1·9		31·2	42	0·1	0·3
0·19		3·1	10	0	—
× 0·019		0·3	0·8	0	—

On the basis of this work we studied a simple symptom of mutation, the production of necrotic lesions on a tobacco variety (Java) on which the untreated strain produces chlorotic lesions only. Virus or isolated ribonucleic acid was treated with nitrous acid. After times *t*, samples were diluted to a constant concentration for assay on Xanthi and Java tobacco plants. The conditions and results are given in Table 1. The total concentration *n* of infective particles was measured by the number of lesions on Xanthi, and of chlorotic and necrotic lesions on Java tobacco, as compared with standard dilution curves. *n* decreases exponentially with *t*:

$$n = n_0 \exp(-t/\tau) \quad (1)$$

where τ is the average time for one lethal conversion of a base per ribonucleic acid molecule.

The necrotic lesions on Java tobacco are due to mutated particles, and their number is expected to be nearly proportional to their concentration *m*. If the alteration of a single base is mutagenic, and if the average number of such mutations per ribonucleic acid molecule in the time τ is *p*, the concentration of such mutants is:

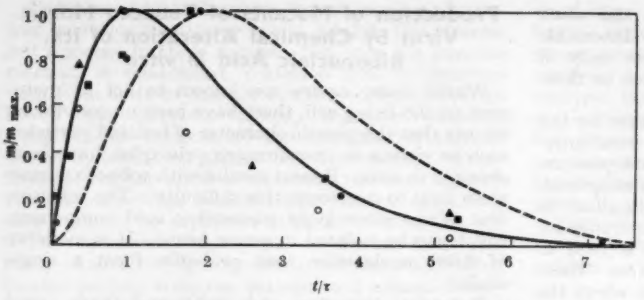

Fig. 1. Dependence of the concentration of mutants (number of necrotic lesions on Java tobacco, relative to maximum value) on the time of incubation with nitrous acid, related to τ. ———, Single-hit curve (equation 3); – – –, double-hit curve; ▲, tobacco mosaic virus *vulgare* (assayed at 0·7 μgm./ml.); ●, ribonucleic acid from tobacco mosaic virus *vulgare* (assayed at 39 μgm./ml.); ■, ribonucleic acid from tobacco mosaic virus *vulgare* (assayed at 19 μgm./ml.); ○, ribonucleic acid from light-green strain *B*11 (assayed at 9·5 μgm./ml.)

$$m = n_0 p \frac{t}{\tau} \exp(-t/\tau) = np\frac{t}{\tau} \qquad (2)$$

or in terms of the maximum value of m:

$$\frac{m}{m_{\max.}} = e\,\frac{t}{\tau}\exp(-t/\tau) \qquad (3)$$

Fig. 1 represents measurements under different conditions with tobacco mosaic virus and with ribonucleic acid derived from two strains. For each case, τ was determined experimentally, using equation (1). The numbers of necrotic lesions on Java tobacco, divided by the maximum value reached in time t, were plotted against t/τ. The experimental results were in agreement with the theoretical relation (3).

The results lead to the following conclusions.

(1) Ribonucleic acid and tobacco mosaic virus treated with nitrous acid give rise to a much larger number of necrotic lesions on Java than untreated material assayed at the same concentration; it is twenty times the spontaneous level when total infectivity has dropped to only half the original value (Table 1). This appearance of mutants at low rates of inactivation excludes selection, and cannot be due to pre-existing mutants, or to mutants arising in the plant.

(2) The mutagenic effect on tobacco mosaic virus and on its isolated ribonucleic acid is equal when the fraction of bases altered in the ribonucleic acid, measured by t/τ, is the same. Also, tobacco mosaic virus treated with nitrous acid has the same proportion of mutants as ribonucleic acid isolated after the treatment. Thus, the mutants are produced by chemical reactions with ribonucleic acid rather than by aggregation phenomena, or by changes in the protein.

(3) The production of mutants is at first linear with t and follows a single-hit curve, irrespective of varying conditions (Fig. 1). Therefore, alterations of single nucleotides are mutagenic.

At $t = \tau$, where one out of about 3,000 nucleotides is altered[2], 6 per cent of the primary infections on Java plants infected with *vulgare* are found to be necrotic (Table 1). If the plating efficiency is assumed to remain unchanged upon mutation, the alteration of any one out of 180 of the total 6,000 nucleotides in the ribonucleic acid strand would be mutagenic, leading to necrotic lesions on Java; this assumption may be subject to later correction.

(4) A variety of other mutants is also produced by nitrous acid. In order to detect them, we isolated individual lesions produced by ribonucleic acid treated with nitrous acid on Xanthi tobacco ($t/\tau = 5{\cdot}2$, Table 1) and assayed them on Java and Samsun plants. Out of 60 lesions, 20 produced no infection, 33 led to a variety of altered symptoms and only 7 gave apparently unchanged symptoms on Samsun tobacco. The altered symptoms proved genetically stable in a transfer experiment. From a control dilution of untreated ribonucleic acid, 64 out of 65 lesions produced infection and no altered symptoms were detected.

We are led to conclude that the chemical alteration of individual bases of the ribonucleic acid molecule *in vitro* is mutagenic. A variety of different mutants may be produced in this way. It remains undecided which of the three types of chemical change caused by the nitrous acid (see above) are mutagenic, and how the chemically altered ribonucleic acid is related to its progeny. In the case of a conversion of cytosine into uracil, it is conceivable that the altered ribonucleic acid undergoes identical reproduction in the host cell.

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Correlated Failure of Synthetic Activities in a Wheat Chromosome

The process of chromosome condensation during meiotic prophase, with its uniformity and synchronization of all parts of the nucleus, provides evidence in support of the genotypic control of chromosome behaviour. So characteristic is this co-ordinated development that any exceptions to it have been considered as due to a basic differentiation of chromosome material into euchromatin and heterochromatin[1]. I have, however, shown recently[2] that the normal synchronized condensation of chromatin threads in the pollen mother cells of perennial ryegrass can be induced to break down by experimental means. This and the other induced changes which affect nucleolus organization have provided evidence pointing to a common control of metabolic activities in chromosomes. In the present experiment, the

uniformity characterizing the behaviour of chromosomes in bread wheat has been observed to break down, though the techniques involved here are of a very different nature.

In the New Pusa wheat variety 797, meiosis is entirely regular except for the occurrence in some of the plants of one or rarely two small chromosome fragments in many of their pollen mother cells. Ahuja (personal communication, 1957), who analysed a large number of plants, found that the "fragments nearly always lie away from the nucleolus". Neither the pollen fertility nor the regular behaviour of chromosomes, however, is found to be affected because of the presence of fragments which obviously owe their origin to spontaneous chromosome breakage. During the course of some mutation-breeding experiments, a number of seeds of this variety were treated with an X-ray dose of 10,000 r. (50 kV.) after soaking in water for 24 hr. The X_2 progeny raised from one of these seeds consisted of plants having one or more fragments in their pollen mother cells, some of them also having a multiple association resulting from reciprocal translocations of chromosomes.

In a number of plants showing such breakage, either a single fragment or two were found to be closely associated with the nucleolus in a very large number of cells (Fig. 1). The consistency with which this association was observed naturally suggested that the nucleolar-organizing region of one of the nucleolar chromosomes might be forming part of the fragment. The suggestion is supported by the presence of a constriction in it and also of a heteromorphic bivalent close to the nucleolus which, however, is not always clearly seen. It is further supported by observations on the root-tip chromosomes of X_2 seedlings, some of which show the presence of only three chromosomes with secondary constrictions in their nuclei (Fig. 2), in contrast to the four invariably found in the control material.

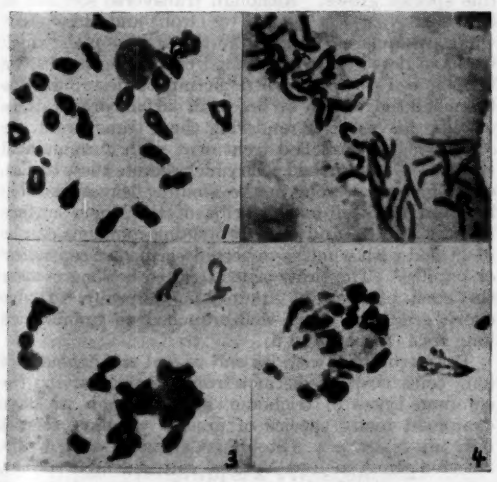

Fig. 1. 1, Pollen mother cell with two constricted fragments, one attached to the nucleolus. Of the 21 II, one close to nucleolus appears heteromorphic. 2, Root-tip cell showing the presence of only three chromosomes with secondary constrictions. 3, An affected pollen mother cell at diakinesis with one of its chromosomes uncondensed. 4, Another cell showing a fragment associated with the nucleolus and two univalents, one of which is retarded. 1,3,4, Carnoy-acetocarmine squashes (× 770, 816, 810); 2, Feulgen squash (× 630)

The organization of the nucleolus by the organizer-carrying fragment is scarcely of any great significance in itself; it was found, however, in a number of plants showing such organization, that either a single chromosome or a pair are retarded in their prophase condensation in a few of the pollen mother cells. This non-synchronized development results in the presence in the same nucleus of chromosomes which present a highly condensed appearance typical of metaphase, and one or two others which are relatively unspiralized, showing poor stainability both with carmine and the Feulgen stains (Figs. 3 and 4). The retardation affects only one of the 21 chromosome pairs and then only in few of the pollen mother cells.

It is not possible from the present observations alone to establish clearly the identity of the chromosome which shows retarded development. The earlier work on rye grass[2], however, strongly suggests that it must be the one which has its nucleolar-organizing region removed by breakage. In rye-grass, it has been shown that following high-temperature treatment, the nucleoli are organized adventitiously on each of the seven chromosomes. If, however, one or more of them fail to take part in nucleolar synthesis, they are invariably retarded in their prophase development. In the case of wheat, it is reasonable to suppose that a chromosome which has a particular site in it differentiated for the formation of nucleolus, may suffer in the synthesis of nucleolar material in the absence of this region; even though it is obvious from the work on rye-grass as well as from other studies[3,4] that an organizer is not always indispensable for nucleolar formation, its main function probably being to collect materials from all other chromosomes also rather than to synthesize them exclusively.

If it is accepted that the retarded chromosome in wheat is invariably the one which fails in its nucleolar synthesis in the absence of its organizing region, it follows that nucleolar formation and chromosome condensation are related phenomena. Since the prophase condensation of chromosomes is known to be conditioned by deoxyribonucleic acid—the Feulgen reaction of the affected chromosome is in agreement with this—the argument can be extended to suggest that the synthesis of deoxyribonucleic acid and nucleolar material in a chromosome are closely correlated.

A possible explanation of this relationship is suggested by the observations of Caspersson[5], Beermann[6] and others, which indicate that the nucleolar material represents the accumulated primary gene products. It is not unlikely that the factors which affect the capacity of the genic material to synthesize its primary products at telophase would also affect its own reproduction during later stages.

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Transmission of Phenotypic Variability within a Pure Line

In the course of a study of the genetic and environmental factors controlling heat resistance in peas (*Pisum sativum*), it was found that when the source of pollen was non-uniform with respect to the environment under which it was developed, the F_1 population exhibited a variance in growth which exceeded considerably that of either parent. Upon analysis of the results it was found that the excessive variance could be attributed entirely to the difference among the environments of the different pollen sources. This suggested that there may be a carry-over by the pollen of environmental influences on the pollen parent.

Two inbred lines of peas were used in these experiments, both lines having been inbred since the early 1930's. It is therefore most likely that these two lines, which have gone through an intensive inbreeding and selection programme extending for some 20–25 years, are for all practical purposes homozygous. All the experiments were performed in the Earhart Plant Research Laboratory. A description of this Laboratory and the experimental facilities available in it has been given by Went[1].

The seeds of both varieties were planted in either constant temperature – artificial light chambers, or in controlled fluctuating temperatures in greenhouses with natural light supplemented by artificial light to make a 16-hr. photoperiod. The temperature fluctuation of the greenhouse consists of a constant temperature during the day period and a constant but lower temperature during the night period.

Crosses were made between the two varieties used in these experiments and within each variety. The crosses were made in the following manner. The plants used as females were grown in a greenhouse with 16-hr. photoperiod and a controlled day temperature of 20° C. and a night temperature of 14° C. These plants were pollinated with pollen from plants growing in different constant temperatures. The F_1 progenies from these crosses were grown at 26° C., 16-hr. photoperiod, to test for heat resistance. It was during this phase of the experiments that differences in the growth characteristics among members of the F_1 population were observed. These differences are related to the temperatures in which the pollen donors had grown.

Table 1 summarizes the results of one experiment and shows the manner in which the crosses were made. A significant difference among pollen sources is shown by the significant differences in the growth behaviour of the three different groups.

Table 2 is a summary of the analysis variance of four separate experiments. In each experiment the contribution to the total variance caused by differences in pollen source, is significant.

Table 1. The Effect of Growth Temperature of the Pollen-donor on the Growth Characteristics of the F_1 Progeny grown at 26° C. All plants grown on a 16-hr. photoperiod. Female Parents grown at 20° C. during Light Period, 14° C. during Dark Period

Pollen-donors grown at: Deg. C. during light period	Deg. C. during dark period	Growth of F_1 progeny: No. of nodes formed	Growth-rate (cm./day)	Final height (cm.)
20	14	14	0·544±0·018	7·68±0·18
14	14	11·6	0·609±0·016	8·45±0·10
26	26	12	0·679±0·032	9·38±0·24

Table 2. Analysis of Variance
Summaries showing effects of differences in growth temperatures among pollen parents on the growth-rates of their progeny

Source	Exp. I Unica × Unica d.f.	M.S.	Exp. II Unica × L_5 d.f.	M.S.	Exp. III L_5 × L_5 d.f.	M.S.	Exp. IV L_5 × Unica d.f.	M.S.
Between pollen sources	3	2·67*	2	3·19*	4	1·51†	1	6·48*
Within pollen sources	20	0·32	9	0·16	20	0·49	7	0·27

* Significant at 1 per cent level. † Significant at 5 per cent level.

These experiments, along with others[2] which have shown that differences can be produced in the growth characteristics of pea plants as a result of the effect of the environment on previous generations, are remarkably similar to those reported by Durrant[3] in flax.

Further studies of the relationship between the previous environment and the effect on the progeny are in progress and will be reported in due course. This work was supported by a grant from the National Science Foundation, Grant No. *G*1385.

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Silicification of Branched Cells in the Leaves of *Nardus stricta* L.

Attention has been directed[1] to the presence of certain peculiar branched rods of opaline silica in the leaves of *Nardus stricta* and in the soils on which this species grows. Although transverse sections of leaves of *N. stricta* figured by Grob[2] and Hegi[3] show what are apparently the minute hat-like opals which we have detected even in the very young leaves, we have found no reference depicting or describing the branched rods which we detect in surface preparations of older leaves after rendering them transparent, for example, by controlled treatment with chromic acid (Fig. 1). The branched cells which secrete these bodies, although not present in the seedling leaves, develop later on the well-marked ribs of the upper surface (Figs. 2 and 3), and their protruding portions can be identified with what have been described as asperities[4] or papillæ[2]. The protrusions tend to be longest near the crest of the rib, diminishing laterally to give every gradation from well-branched to unbranched long cells (Figs. 4 and 5).

This structure, with its end-to-end arrangement of long cells, is quite distinct from those involving the common types of trichome, and although we have examined many species of grasses we have seen it only in *N. stricta*. Stebbins[5] suggests that a distinctive genus such as *Nardus*, with its single species, may represent the last remains of some evolutionary line now almost extinct, or the culmination of a trend which has been successful in one specialized sphere. If it should be confirmed that no other grass besides *N. stricta* exhibits these branched cells and branched opaline bodies, it would give additional support to such theories.

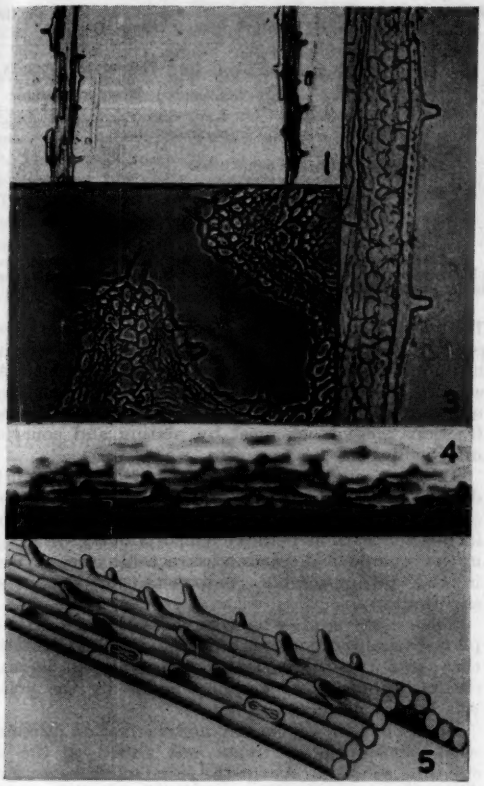

Fig. 1. *Nardus stricta*. Branched rods of opal in two ribs of the upper surface of the leaf (× 100). Fig. 2. Transverse section (× 270). Fig. 3. Longitudinal section (× 270). Fig. 4. Rows of branched cells in one rib, darkened by chromic acid treatment (× 220). Fig. 5. Diagrammatic representation of surface cells in one rib

The progressive silicification of *Nardus* leaves is being further investigated with material collected at intervals throughout the year. The special techniques used in this work have already been described[6].

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Alary Polymorphism in the Gerroidea (Hemiptera Heteroptera)

The Gerroidea exhibit a marked alary polymorphism which has promoted many investigations since that of Poisson[1], who classified the various forms and attempted to investigate the genetics of this polymorphism by breeding experiments. This lead was followed by Ekblom[2] and Guthrie[3] without reference to Mitis[4], who had suggested a possible link between life-cycles and polymorphism. These breeding experiments have given varied and confusing results, and one may only conclude that any form can give rise to any other and that, as Guthrie[3] decided, the problem is not one of simple genetics.

In a recent study of the biology of *Gerris* and *Velia* species, I have been able to extend the observations made by Mitis[4], illustrating a close relation between life-cycle, habitat and polymorphism[5]. Only bivoltine species were seen to be polymorphic, the univoltine species being predominantly monomorphic. Of the univoltine species, *Gerris najas* (Deg.) and the *Velia* species are most commonly apterous and usually inhabit running water, whereas the monomorphic univoltine species inhabiting ponds and pools (*G. costai* (H.-S.), *G. gibbifer* Schum.) are mostly macropterous. In these instances it seems that the needs of distribution have determined the form of the single generation. Poisson[1] showed that short-winged forms were more abundant in the summer, and I have found that they are restricted to the summer generation in most cases. *G. argentatus* Schum., *G. odontogaster* (Zett.) and *G. thoracicus* Schum. exhibit an alternation between a macropterous overwintering generation and a polymorphic summer generation, while *G. paladum* appears to have an entirely short-winged summer generation. Two further species (*G. lacustris* (Linn.) and *G. lateralis* Schum.) resemble *G. odontogaster* but have in addition a small proportion (less than 10 per cent) of short-winged forms in the over-wintering generation.

All these species spend the winter months on land as adults, flying to and from over-wintering sites in the autumn and spring respectively. Having established themselves on suitable habitats these insects then resorb their wing-muscles and breed, producing in most instances a mixed generation of long- and short-winged forms. The species that do this occupy small ponds, pools and ditches or limited areas of lake-fringes. Since short-winged forms contain the same number of eggs as long-winged forms, and they both grow at the same speed[5], the usual theories of the significance of short-wingedness are no longer adequate. Instead I wish to stress the inability of short-winged forms to fly—an obvious but neglected point of view. It has been noted that long-winged forms lose their powers of flight after over-wintering and before breeding, as in many insects. The following generation consists of approximately equal numbers of flightless forms, which maintain the breeding population on the pond on which the species has already bred successfully, and alate forms which are capable of migration if the pond becomes either over-populated or a poor habitat (due to surface pollution, drought, etc.). In this context it should be recalled that *G. paludum* has an entirely short-winged summer generation, but inhabits the open water of lakes and large ponds and is not therefore exposed to the same selective pressures as described above. The alternation of a long-winged and a polymorphic or short-winged generation reflects the alternation of habitats occupied by the insect[3].

Ford[6] described three ways by which a balanced polymorphism such as this could be maintained: switching by simple genic segregation (as in *Sitona*[7]), selective predation alternately favouring one form and then the other, where both forms are produced in each generation (as in *Adalia*[8]), or by the switching of a gene complex by environmental factors. Mather[9] regarded the last method as the simplest system

which could produce the situation in which types "successively vanish and reappear in a population", as I have observed to occur in these insects.

This approach to an old problem will be described in greater detail elsewhere, but it would seem that the results of previous breeding experiments must be largely discounted on the grounds that the offspring produced from any one form varies from one generation to the next, and most authors combine the results of breeding experiments made throughout the season. As the polymorphic form resulting from each breeding is probably influenced by the environment, the laboratory conditions should be carefully controlled. We are now in a position to select a species with a distinct 'alternation of generations' and attempt to operate the switch mechanism by such controlled breeding.

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Carbon Dioxide Fixation in Germinating Pine Pollen (*Pinus ponderosa*)

Carbon dioxide fixation by plant tissues other than those involved in photosynthesis has recently been reported for whole plant tissues and cellular particulates of roots[1,2]. This communication reports observations on the incorporation of carbon dioxide into the organic acid, amino-acid, and protein fractions of germinating pine pollen.

Pinus ponderosa pollen was germinated for 15 hr. at 29° C. in 0·01 *M* calcium–potassium phosphate buffer, *p*H 5·9, in the presence of the fungistat – bacteriostat mixture 'Mysteclin' (an antibiotic – antifungal mixture composed of tetracycline and mystatin; kindly supplied by the Medical Division, E. R. Squibb and Sons, New Brunswick, New Jersey). Radioactive potassium bicarbonate was added, and then the mixture was shaken for 1 hr. in a Warburg flask at 25° C. The reaction was stopped by acidification and the excess carbon dioxide removed by bubbling through inert carbon dioxide for 15 min. The mixture was then centrifuged and the supernatant removed from the pollen residue.

Table 1. Percentage of Carbon-14 Dioxide Incorporated by *Pinus ponderosa* Pollen

Experiment	In supernatant		
	Total	Ether extract	Alcohol extract
1	24·6	11·2	2·1
2	34·1	13·1	3·4

Reaction mixture contained 200 mgm. pollen germinated 15 hr., 29° C.; 0·8 mgm. 'Mysteclin' in 0·002 *M* potassium phosphate buffer, *p*H 5·9. 0·5 μmoles potassium bicarbonate containing 125,000 counts/sec. was added after equilibration. The side-arm contained 0·5 ml. 2 *N* sulphuric acid added after 1 hr. incubation. Total volume, 2·5 ml.; temperature, 25° C.; incubation time, 1 hr.

Table 2. Effect of Phosphoenolpyruvate on Carbon-14 Dioxide Fixation by Germinating Pollen (*Pinus ponderosa*)

*p*H	Treatment	Percentage carbon-14 dioxide activity incorporated into	
		Supernatant	Residue
4·8	Heat inactivated	0·3	0·0
	Without phosphoenolpyruvate	9·0	0·6
	With phosphoenolpyruvate	10·7	0·5
7·4	Heat inactivated	0·3	0·0
	Without phosphoenolpyruvate	11·8	0·7
	With phosphoenolpyruvate	13·8	0·7

Reaction mixture the same as under Table 1 except 7 mgm. phosphoenolpyruvate was added where indicated; 90 μmoles phosphate buffer in each individual flask.

The total amount of radioactive carbon dioxide incorporated was determined by measuring the activity in aliquots of the supernatant and the residue. An ether extract and an alcohol extract of the reaction mixture were prepared. Activities in each of these fractions were ascertained by plating and counting in a windowless flow counter.

Table 1 indicates that most of the carbon-14 dioxide incorporated was in acid- or water-soluble components in the supernatant solution. After 1 hr. incubation, carbon-14 dioxide incorporated was higher in the organic acid fraction extractable in ether than in the alcohol-soluble components of the pollen supernatant.

Since many studies have indicated the presence of phosphoenolpyruvate carboxylase in plant tissues[3], the capacity of phosphoenolpyruvate to increase the incorporation of carbon dioxide by the pollen was investigated.

As Table 2 shows, carbon dioxide fixation increased when phosphoenolpyruvate was added to the incubating solution. About the same increase occurred whether the incubating medium was at the optimal *p*H of the phosphoenolpyruvate carboxylase or closer to the physiological *p*H. This agreement may be due to the high internal buffering capacity of the whole cell. The optimum *p*H for *P. ponderosa* pollen germination is 5·9, and germination is inhibited below *p*H 5·0 and above *p*H 7·0. This fact probably explains the total lower incorporation in the results shown in Table 2 as compared with those in Table 1. The stimulation due to phosphoenolpyruvate noted in particulate preparations[3] was much larger than that observed here. Since the inherent levels of phosphoenolpyruvate in pollen are quite high, perhaps alternate mechanisms of carbon dioxide fixation exist in germinating pollen or the treatment procedure used may not be optimal.

The pollen residues, which were insoluble in alcohol and ether, were hydrolysed overnight in 6 *N* hydrochloric acid at 117° C. Two-dimensional paper chromatograms were prepared of the alcohol extract of the hydrolysate using phenol/water and butanol/propionic acid/water as the solvents. The radioautographs showed activity in serine, aspartate, glutamate and malate. Radioautographs of the ether extract of the supernatant showed activity in malate, in what appeared to be citrate and in another organic acid.

The net synthesis of labelled amino-acids and possibly protein by germinating pollen, as evidenced by the hydrolysate studies, indicates that pollen on germinating into the female tissue not only absorbs water and activates inherent enzyme systems but probably can also synthesize the protein constitutive units of enzymes. Since pollen generally grows in a highly anaerobic environment, the capacity of pollen

to incorporate carbon dioxide and synthesize amino-acids, proteins and possibly cell-wall materials may be an important growth mechanism in the plant reproductive cycle. The reduction and incorporation of carbon dioxide, coupled with the oxidation of carbohydrates present in the female gametophyte tissue, may in part be the mechanism by which rapid tube elongation can occur in pollen grains with only very limited carbon substrates.

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Effect of the Cotton Plant in the Sudan Gezira on Certain Leaf-feeding Insect Pests

COTTON in the Sudan Gezira, where some 240,000 feddans (1 feddan = 1·034 acres) of *Gossypium barbadense* L. are grown by gravity irrigation from the Sennar Dam, is attacked, particularly during the first 3½ months of its growth, by three important leaf-feeding insects, namely, the jassid, *Empoasca libyca* de Berg.; whitefly, *Bemisia tabaci* Gen. and thrips, *Hercothrips fumipennis* Bag. and Cam.[1]. These insects may cause important loss in yield of seed cotton[2], but their intensity of attack varies from season to season[2,3]. If, however, application of control measures is delayed until damage is easily visible, yield benefit from such control may be seriously reduced[2]. An object of entomological research is prediction of outbreaks of economic significance.

One cause of the seasonal variations in numbers was elucidated recently by a study of the effect of nitrogenous fertilizer on these pests. In an experiment in which 1 N. or 2 N. (where 1 N. is equivalent to 45 rotls of nitrogen; 1 rotl = 0·99 lb.) per feddan as ammonium nitrate was applied to cotton at different dates during the first 3½ months after sowing, it was found that the estimated Kjeldahl nitrogen in the dry matter of the foliage of plants receiving fertilizer was greater than in those not receiving fertilizer. Nevertheless, there was a tendency in all investigated treatments for the concentration of leaf nitrogen to fall as the season progressed, while infestations of jassids and whitefly increased with time. When, in an analysis of covariance, these latter effects were eliminated, a highly significant regression of jassid and whitefly densities on concentration of leaf nitrogen could be demonstrated. This finding is reminiscent of the work of Allen and Selmon[4] on *Phaedon coclleariae* F., and Le Roux[5] on *Tetranychus bimaculatus* Harvey, to quote two recent examples, and it is believed to be due to an increase in birth-rate with increased concentration of leaf nitrogen.

Table 1. MEAN NITROGEN CONCENTRATION IN COTTON LEAVES (PER CENT OF DRY WEIGHT) IN FIVE SAMPLES TAKEN BETWEEN EARLY SEPTEMBER AND LATE OCTOBER DURING FOURTEEN SEASONS

Locality	0 N. plots	3 N. plots	Mean
Hag Abdulla (south)	3·51	3·70	3·60
Gezira Research Farm (centre)	3·70	3·84	3·77
Turabi (north)	3·87	3·98	3·93
Mean	3·69	3·84	3·76

	Sites	Nitrogen
S.E.	±0·049	±0·059
Least sig. diff.		
(P = 0·05)	0·14	0·17
(P = 0·01)	0·18	0·22

Examination of results obtained by the Research Division on concentration of leaf nitrogen at three Gezira sites over fourteen seasons gave the means shown in Table 1.

The concentration of leaf nitrogen was affected by locality and fertilizer treatment. The effect on the two main Gezira cotton varieties, namely, *X*173*OA*, grown in the south, and Domain Sakel, grown in the north, was insignificant. There were also highly significant seasonal differences. Because of the established effect on Gezira cotton yields[6] of rains falling between July 1 and August 15 (pre-sowing rains) the covariance of concentration of leaf nitrogen on these rains was examined during the six seasons when all the cotton had been sprayed with DDT. The correlation coefficient of concentration of leaf nitrogen on pre-sowing rains was − 0·5842 which, for 22 degrees of freedom, is highly significant. There was evidence, however, that the effect was not direct, and seasonal variation in concentration of leaf nitrogen was caused by some uninvestigated factor itself correlated with rainfall.

The regression of the mean September and October concentration of nitrogen in the leaf material of the cotton plant on pre-sowing rains could be expressed by the equation:

$$\bar{X}_2 = 4{\cdot}07 - 0{\cdot}0031X_1$$

where $\bar{X}_2$ is the mean concentration of leaf nitrogen during September and October (as percentage of dry matter), and X_1 is the rainfall in mm. during July 1–August 15. The standard error of the regression coefficient is ± 0·0009).

The seasonal incidence of pests feeding on the leaves was recorded during four seasons at one site (Gezira Research Farm), and was found to be correlated with pre-sowing rains and the concentration of leaf nitrogen. The regression equation for rate of jassid increase is:

$$a = 18{\cdot}03 - 0{\cdot}071X_1 \ (\pm 0{\cdot}010)$$
$$a = 10{\cdot}96\bar{X}_2 \ (\pm\ 0{\cdot}69) - 35$$

where a is the mean rate of increase in jassid nymphs per 100 leaves per day

(other symbols as before, with standard errors of regression coefficients in brackets). This describes the rate of increase during September and October before spraying as well as that during October and November after DDT spraying.

The mean infestations during October and November, namely, after spraying, and at a time when the pests are considered to exert most effect on crop yields, were:

Jassids: $Y_1 = 156{\cdot}4X_2 - 478$ ($\pm$ 20·4)

Whitefly: $Y_2 = 9{\cdot}71X_2 - 0{\cdot}27$ ($\pm$ 0·17)

Thrips: $Y_3 = 4{\cdot}16X_2 - 0{\cdot}89$ ($\pm$ 3·17)

where Y_1 is the mean number of nymphs of *E. libyca* per 100 leaves, Y_2 is the mean number of adults of *B. tabaci* (logarithm), and Y_3 is the percentage of leaves infested with larvæ of *Hercothrips* sp. (arc sin/percentage) (other symbols as before).

The regression coefficients for whitefly and jassid infestations were highly significant: that for thrips was not significant.

E. libyca is preyed upon by the Mymarid egg parasites *Anagrus* sp. and *Paranagrus* sp. while the *Aphelinid* parasites *Eretmocerus* sp. and *Prosaptella* sp. cause heavy mortality of the later instars of *B. tabaci*. All these parasites appear to be more numerous in seasons of good than of poor pre-sowing rains, but statistical evidence is deficient.

The results, although incomplete, raise the interesting possibility that the cotton plant in the Sudan Gezira may, by the seasonal changes in composition of its foliage expressed by percentage of Kjeldahl nitrogen, influence the rate of increase of some of its leaf-feeding insects in such way as to enable them to 'break away' from biological controlling agents. According to F. Crowther[7] the concentration of nitrogen in cotton leaves is determined by: (1) the concentration of nitrogen in the soil and (2) the rate of development of the plant. Jewitt[8] showed that the nitrate nitrogen in Gezira soils was negatively correlated with pre-sowing rains. The results so far available do not indicate that rains control leaf nitrogen directly, but determine it through other correlated factors influencing the early rate of development of the cotton plant.

It is hoped that this knowledge, considered in relation to some other aspects of the ecology of the pests concerned, will enable prediction to be made of pest outbreaks in the Sudan Gezira before the crop is sown. A full account of this approach in relation to the cotton jassid will be published elsewhere.

I am grateful to Sayed Ahmed Kordofani, of the Research Division, for access to his records of the growth and composition of the cotton plant in the Sudan Gezira, and to the Chief of Agricultural Research, Ministry of Agriculture, Sudan Republic, for permission to publish this work.

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Bat Erosion as a Factor in Cave Formation

I have read with much interest the communication by W. A. King-Webster and J. S. Kenny[1] in which it is suggested that roosting bats can play a considerable part in cave excavation where the rock is soft. In particular, reference is made to the existence, in the roof of a limestone cave in Mt. Tamana (Trinidad), of bell-shaped cavities ranging in depth from 3 ft. to 6 ft., and in diameter at the mouth from 1½ ft. to 2½ ft., and which are used by sleeping bats. The suggestion is made that the habit of the bats of alighting at the lower edge of the bell and then jostling upwards into a central position, by continuation over innumerable years, has led to the excavation of these cavities, with maximum removal of rock at the mouth of the bell.

Ceiling cavities of the type described are, however, a commonplace feature in many limestone caverns, and indeed in portions of those caverns that have never been known to have been used by bats. This applies particularly to tunnels so far in linear distance from the cave entrance or in depth below it that they are beyond the normal zone of penetration of the bats. Such ceiling pockets, and also similar indentations in cave walls, have been described by Bretz in his classic paper[2], in which he elaborates on the theories, originally proposed by Davis[3], concerning the phreatic origin of certain types of cave tunnels and systems. Bretz specifically quotes such wall and ceiling pockets as examples of cave features of phreatic origin, pointing out that it is difficult to visualize their formation by any solution mechanism under conditions whereby there was an air space above the water surface. He therefore considers that such ceiling pockets were formed below the lowest normal water-table level (such as might occur at times of drought) and he directs attention to the fact that if the 'eating-out' process is continued long enough, adjacent pockets merge into one another, thus producing one of the effects described by King-Webster and Kenny.

During the course of the studies made by my wife and myself on the habits of certain cave-dwelling bats[4], in particular, the greater horseshoe bat (*Rhinolophus ferrumequinum*), we have often noticed ceiling pockets, of the type described above, in the natural caverns that exist in scattered outcrops of Devonian limestone, in the neighbourhood of Buckfastleigh in Devon. Some of these pockets are commonly used during the winter months by the greater horseshoe bats, probably because such dome-shaped cavities provide areas of roof that are free from draughts. It is, however, important to note that these caves were only revealed as a result of quarrying operations during the past century, and they were thus not occupied by bats until they were opened to the outside world, barely a hundred years ago. Although we have evidence in Devon that the claws of a greater horseshoe bat can mark the roof of a cave, at least to the extent of scratching off powdery surface deposits from the limestone, it would be surprising indeed if the colonies of bats could have excavated roof pockets to a depth of several feet in such a limited time. I therefore feel that although the 'bat erosion' effect postulated by King-Webster and Kenny may well occur with certain types of limestone, it represents at best only a secondary, and probably minor, contribution to the shape and size of the ceiling pockets described.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, November 24

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Lieutenant C. J. Wynne-Edwards, R.N.: "Hydrographic Survey in the Falkland Islands Antarctic Dependencies".

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE (in the Council Room of the Science Museum, Exhibition Road, South Kensington, London, S.W.7), at 5.30 p.m.—Dr. G. J. Whitrow: "The Evolution of Our Numerals and System of Numeration".

INSTITUTION OF ELECTRICAL ENGINEERS, RADIO AND TELECOMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. J. S. Seeley and Dr. J. Brown: "The Use of Dispersive Dielectrics in a Beam-Scanning Prism"; Dr. J. S. Seeley: "The Quarter-Wave Matching of Dispersive Materials"; Mr. A. Carne and Dr. J. Brown: "Theory of Reflections from the Rodded-Type Artificial Dielectric".

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. C. A. Rogers: "Packing and Covering".* (Inaugural Lecture.)*

ROYAL AERONAUTICAL SOCIETY (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 6 p.m.—Mr. J. E. Pateman: "Inertia Guidance".

Tuesday, November 25

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. H. E. Rose: "A Suggested Equation Relating to the Mixing of Powders and its Application to the Study of the Performance of Certain Types of Machine".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. E. H. Mercer: "Electron Microscopy and the Structure of the Living Cell".* (Eighth of eleven lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation. Further lectures on November 27 and December 2 and 4.)

SOCIETY OF INSTRUMENT TECHNOLOGY, DATA PROCESSING SECTION (at Manson House, Portland Place, London, W.1), at 6 p.m.—Mr. R. C. M. Barnes: "Digital Data-Recording for Nuclear Experiments".

SOCIETY FOR ANALYTICAL CHEMISTRY, PHYSICAL METHODS GROUP (at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 6.30 p.m.—Fourteenth Annual General Meeting, followed by meeting on "Modern Methods of Purification".

Wednesday, November 26

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. H. M. Sinclair: "Essential Fatty Acids".*

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. Graham F. Elliott: "Fossil Calcareous Algal Floras of the Middle East"; Miss Leonora A. Stevens: "The Interglacial of the Nar Valley, Norfolk" (paper communicated by Dr. R. G. West).

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Prof. Max Mallowan: "Excavations at Nimrud, 1958".

INSTITUTE OF MARINE ENGINEERS (at the Memorial Building, 76 Mark Lane, London, E.C.3), at 5.30 p.m.—Sir John Cockcroft, O.M., F.R.S.: "Recent Advances in Nuclear Engineering" (Sir Charles Parsons Memorial Lecture).

INSTITUTION OF ELECTRICAL ENGINEERS, SUPPLY SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. L. L. Alston and Prof. F. M. Bruce: "Investigations of Power-Follow Current Phenomena using a Synthetic Power Source"; Dr. L. L. Alston: "The Impulse Initiation of Arc Discharges".

BRITISH INSTITUTION OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6 p.m.—Annual General Meeting. 7.15 p.m.—Prof. E. E. Zepler: Presidential Address.

SOCIETY OF CHEMICAL INDUSTRY, FOOD GROUP (at 14 Belgrave Square, London, S.W.1), at 6.15 p.m.—Scientific Papers.

BRITISH PSYCHOLOGICAL SOCIETY, MEDICAL SECTION (at the Royal Society of Medicine, 1 Wimpole Street, London, W.1), at 8.30 p.m.—Mr. John Bowlby: "Studies of Parent–Infant Interaction in Man and Animals—some Notes on Projects in Progress".

Thursday, November 27

INSTITUTE OF PHYSICS, ELECTRON MICROSCOPY GROUP (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 10 a.m.—Meeting on "Electron Staining".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. Michael Abercrombie: "Cell Surface and the Control of Growth".* (Ninth of eleven lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation. Further lectures on December 2 and 4).

Friday, November 28

INSTITUTE OF PHYSICS, ELECTRON MICROSCOPY GROUP and X-RAY ANALYSIS GROUP (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 10 a.m.—Joint Conference on "Precipitation in Alloys".

INSTITUTE OF RURAL LIFE AT HOME AND OVERSEAS (at Friends International Centre, 32 Tavistock Square, London, W.C.1), at 1.15 p.m.—Mr. George Bredin: "The Impact of the Gezira Cotton-Growing Scheme on the Rural Population of the Blue Nile".*

ROYAL ASTRONOMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.15 p.m.—Geophysical Discussion on "Turbidity Currents: High Speed Underwater Flow of Sediment Suspensions". Chairman: Dr. G. E. R. Deacon, F.R.S. Speakers will include Dr. A. S. Laughton, Dr. R. Stoneley and Dr. T. H. Ellison.

PHYSICAL SOCIETY (in the Large Lecture Theatre, Chemistry Department, Imperial College, Imperial Institute Road, London, S.W.7), at 5 p.m.—Prof. Niels Bohr, F.R.S.: "General Implications of the Atomic Nucleus" (9th (1958) Rutherford Lecture).*

ROYAL ANTHROPOLOGICAL INSTITUTE OF GREAT BRITAIN AND IRELAND (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Prof. Sir Wilfrid Le Gros Clark, F.R.S.: "Bones of Contention" (Huxley Memorial Lecture).

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion Meeting on "Problems Encountered in the Field of Neurophysiology".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. J. Z. Young, F.R.S.: "Squids, Cuttlefishes and Octopuses".

Friday, November 28—Thursday, December 4

ELECTRONIC COMPUTER EXHIBITION (at Olympia, London, W.14).*

Monday, December 1—Wednesday, December 3

Business Computer Symposium.

Saturday, November 29

INSTITUTE OF PHYSICS, X-RAY ANALYSIS GROUP (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 9.30 a.m.—Scientific Papers.

BOTANICAL SOCIETY OF THE BRITISH ISLES (in the Lecture Room of the Royal Horticultural Society, Vincent Square, London, S.W.1), at 12 noon—Exhibition Meeting.

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER, Grade B (with a degree in electrical engineering or physics and preferably a special knowledge or industrial experience of some branch of the subject), IN TELECOMMUNICATIONS AND ELECTRONICS—The Clerk to the Governors, Woolwich Polytechnic, London, S.E.18 (November 28).

ASSISTANT LECTURER (with an honours degree in physics and preferably able to teach the subject to a high standard) IN PHYSICS—The Principal, Wigan and District Mining and Technical College, Wigan (December 1).

LECTURER or ASSISTANT LECTURER (with a good honours degree and teaching experience) IN BIOLOGY at the Royal Technical College of East Africa—The Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2 (December 5).

LECTURER (with special qualifications in botany or agricultural botany) IN BOTANY—The Secretary, West of Scotland Agricultural College, 6 Blythswood Square, Glasgow, C.2 (December 5).

LECTURER or RESEARCH ASSISTANT IN BACTERIOLOGY AND VIROLOGY—The Registrar, The University, Sheffield (December 6).

RESEARCH ASSISTANT (preferably with a Ph.D. degree and suitable experience in biochemistry and microbiology) IN THE DEPARTMENT OF BACTERIOLOGY, to assist in a programme of work on the immunochemistry of *Bordetella pertussis*—The Registrar, The University, Manchester 13 (December 6).

SENIOR LECTURER and a LECTURER IN MATHEMATICS at the University of Auckland, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, December 12).

LECTURER (graduate in metallurgy or chemistry with special qualifications in the theory and principles of extraction metallurgy) IN METALLURGY—The Registrar, The University, Manchester 13 (December 13).

SENIOR LECTURER/LECTURER IN CHEMISTRY at the University of New South Wales, Sydney, Australia—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2 (Australia, December 13).

READER IN AERONAUTICS at Imperial College, London, S.W.7—The Academic Registrar, University of London, Senate House, London, W.C.1 (December 15).

SENIOR LECTURER (registered pharmaceutical chemist) IN PHARMACY at the University of Adelaide, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 15).

CHAIR OF CIVIL ENGINEERING, SENIOR LECTURER or LECTURER IN MECHANICAL ENGINEERING, LECTURER IN ENGINEERING MATHEMATICS, LECTURER IN CIVIL ENGINEERING, and a LECTURER IN ELECTRICAL ENGINEERING at the University of Khartoum—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 29).

CHAIR OF BOTANY—The Registrar, The University, Hull (December 31).

RESEARCH FELLOW IN THE PHYSIOLOGY DEPARTMENT, Faculty of Rural Science, University of New England, Australia, to undertake research associated with a study of the comparative physiology of mammalian erythrocytes with particular reference to the physiological significance of individuality in the ruminant erythrocyte—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 31).

LECTURERS or ASSISTANT LECTURERS IN PHYSIOLOGY at the University of Malaya—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 31).

LECTURER or ASSISTANT LECTURER (preferably with qualifications in mathematical analysis and/or statistics) IN MATHEMATICS at the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 10).

LECTURER IN PURE MATHEMATICS—The Secretary, Queen's University, Belfast (January 15).

BROTHERTON CHAIR OF CHEMICAL ENGINEERING in the Houldsworth School of Applied Science—The Registrar, The University, Leeds 2 (January 31).

ENTOMOLOGIST (with a good honours degree in zoology and an interest in, and aptitude for, taxonomic work, and preferably experience in the Diptera particularly the Calyptrata) at the Commonwealth Institute of Entomology, London—The Secretary, Commonwealth Agricultural Bureaux, Farnham House, Farnham Royal, Bucks (January 31).

BIOCHEMIST (with a Ph.D. degree or equivalent research experience), for work on the metabolism of cell and organ cultures—The Secretary, Strangeways Research Laboratory, Wort's Causeway, Cambridge.

EXPERIMENTAL OFFICER (at least 26 years of age, preferably with a pass degree, or at least H.N.C. (engineering or applied physics) or equivalent), to carry out experiments designed to investigate the mechanical strength of complex assemblies, to instrument parts for experiments and to analyse experimental results—The Senior Recruitment Officer, Atomic Weapons Research Establishment, Aldermaston, Berks, quoting Ref. A.1895/34.

PHYSICAL CHEMIST, PHYSICIST or METALLURGIST, for research on anodic oxide films—Dr. G. M. Shrum, Director, British Columbia Research Council, University of British Columbia, Vancouver 8, B.C., Canada.

READER IN NUCLEAR ENGINEERING at Queen Mary College—The Academic Registrar, University of London, Senate House, London, W.C.1.

RESEARCH ASSISTANT (preferably with a Ph.D. degree in chemistry or biochemistry, for work on the biochemical analysis of *Haemophilus pertussis* antigens—The Secretary, The Lister Institute of Preventive Medicine, Elstree, Hertfordshire.

RESEARCH ASSISTANT, to help with quantum mechanical calculations on tetrahedral and other nearly spherical molecules, using an electronic computer—Dr. R. A. Buckingham, University of London Computer Unit, 44 Gordon Square, London, W.C.1.

RESEARCH FELLOW (with experience in acoustic measuring techniques) IN PHYSICS, for work on materials for use in acoustic assemblies—The Registrar, The University, Leicester.

SENIOR SCIENTIFIC OFFICER/SCIENTIFIC OFFICER (honours graduate with a first- or good second-class honours degree), to undertake research on ceramic fuels for reactors, including the determination of physical and chemical properties over a wide range of temperatures, phase equilibria and investigation of fabrication techniques—The Group Recruitment Officer (1248/34), U.K.A.E.A., Atomic Energy Research Establishment, Harwell, Berks.

SENIOR RESEARCH OFFICER (PLANT PATHOLOGY) (with a good honours degree in botany (plant pathology) and suitable professional and administrative experience), to take charge of the Plant Pathology Division, Department of Agriculture, Kenya, and to guide and direct work of other pathologists in the Division—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/7/015.

SENIOR TECHNICIAN (capable of supervising setting-out of laboratories for physiological, biochemical and histological classes, and a knowledge of workshop techniques) IN THE PHYSIOLOGY DEPARTMENT—The Secretary, Queen Elizabeth College (University of London), Campden Hill Road, London, W.8.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

B.B.C. Engineering Monograph No. 20: The B.B.C.'s Mark II Mobile Studio and Control Room for the Sound Broadcasting Service. By L. E. H. O'Neill. Pp. 23. (London: British Broadcasting Corporation, 1958.) 5*s*. [189

Higher Education in the United Kingdom: a Handbook for Students from Overseas. Revised edition. Pp. 208. (London: Longmans, Green and Co., Ltd., 1958. Published for the British Council and the Association of Universities of the British Commonwealth.) 5*s*. [189

Britain's Future and Technical Education. Pp. 12. (London: Ministry of Education, 1958.) [189

Fifth Report from the Select Committee on Estimates together with part of the Minutes of the Evidence taken before Sub-Committee B and Appendices, Session 1957–58; The Department of Scientific and Industrial Research. Pp. xvi+165. (London: H.M. Stationery Office, 1958.) 9*s*. net. [199

Planning, Vol. 24, No. 426 (19 September, 1958): Problems o World Liquidity. Pp. 201–224. (London: Political and Economic Planning, 1958.) 2*s*. 6*d*. [229

The Future of Mineral Exploration. By Dr. Anton Gray. (Fourth Sir Julius Wernher Memorial Lecture.) Pp. 13. (London: Institution of Mining and Metallurgy, 1958.) [229

Ultra-High-Energy Nuclear Physics. By Prof. C. C. Butler. (Inaugural Lecture delivered 21 January 1958.) Pp. 26+7 plates. (London: Imperial College of Science and Technology, 1958. Distributed by the Modern Book Co., Ltd., 19 Praed Street, W.2.) 5*s*. [229

The Lichenologist, Vol. 1, Part 1. Pp. 48. (Cardiff: A. E. Wade, Secretary, British Lichen Society, c/o National Museum of Wales, 1958.) 20*s*. [229

Forum, Vol. 1, No. 1 (Autumn, 1958). (For the discussion of new trends in education.) Pp. 36. Annual subscription: 8*s*. 6*d*.; Single issues, 3*s*. (Leicester: P.S.W. (Educational) Publications, 1958.) [229

British Electrical and Allied Industries Research Association Technical Report L/T351: The Electrical Properties of Tungsten Trioxide. By J. Hirsch. Pp. 10+2 figures. (Leatherhead: British Electrical and Allied Industries Research Association, 1956.) 10*s*. 6*d*. [229

Polish Cultural Institute. Selective Quarterly Guide to Polish Periodical Literature, Vol. 3, 3, 1958. Pp. 64. (London: Polish Cultural Institute, 1958.) [229

Other Countries

Kungl. Sjöfartsstyrelsen. Jordmagnetiska Publikationer Nr. 18: Charts of Average Geomagnetic Elements D. H. and Z. 1955 0 for Denmark, Finland, Norway, Sweden. 3 charts. (Stockholm: Kungl. Sjöfartsstyrelsen, 1958). [189

Commonwealth of Australia: Department of External Affairs. Australian National Antarctic Research Expeditions. A.N.A.R.E. Reports. Series C, Vol. 1: Terrestrial Magnetism. Magnetic Observations at Heard Island, 1954. By K. B. Lodwick. Pp. v+7+45 tables. Magnetic Observations at Macquarie Island, 1954. By C. S. Robertson. Pp. v+7+53 tables. (Melbourne: Antarctic Division, Department of External Affairs, 1958.) [189

Symposium on Production, Properties and Applications of Alloy and Special Steels held on 1st, 2nd, 3rd and 4th February, 1956. Organized by Dr. B. R. Nijhawan and P. K. Gupta. Pp. vi+488. (Jamshedpur: National Metallurgical Laboratory, 1958.) [189

Indian Mining Journal, Vol. 5 (Special issue): Symposium on Mineral Beneficiation and Extractive Metallurgical Techniques held at the National Metallurgical Laboratory, Jamshedpur, February, 1957. Pp. xxvi+355. (Calcutta: Temple Press, 1957.) [189

Indian Construction News (Special number, February, 1958): Recent Trends in the Field of Production, Practice and Research on Refractories Used in Metal Industries: a Symposium held at the National Metallurgical Laboratory, January 19, 20 and 21, 1955. Organized by B. R. Nijhawan and Rabindar Singh. Pp. 162. (Calcutta: Indian Construction News, 1958.) Rs. 5. [189

Canada: Department of Northern Affairs and National Resources. National Museum of Canada. Bulletin No. 147: Annual Report of the National Museum of Canada for the fiscal year 1955–56. Pp. iii+140 (17 plates). 1.50 dollars. Bulletin No. 150: An Annotated List of the Marine Algae of British Columbia and Northern Washington (including Keys to Genera). By Robert F. Scagel. Pp. vi+289. 2 dollars. Bulletin No. 139: Haida Carvers in Argillite. By Marius Barbeau. Pp. viii+214. 3 dollars. Canadian Mammals. By Auston W. Cameron. Pp. 81. 50 cents. (Ottawa: Queen's Printer, 1957 and 1958.) [189

Ministère du Nord Canadien et des Ressources Nationales. Musée National du Canada. Quelques Oiseaux du Canada. Par W. Earl Godfrey. Planches noires par John Crosby. Pp. 48 (14 planches). (Ottawa: Imprimeur de la Reine, 1957.) 35 cents. [189

Natural History Papers of the National Museum of Canada. No. 1 (August 18th 1958): A Horse Astragalus from the Hand Hills Conglomerate of Alberta. By L. S. Russell. Pp. 3. No. 2 (August 18th, 1958): Champosaur Giants. By W. Langston, Jr. Pp. 4. (Ottawa: Queen's Printer, 1958.) [229

Quarterly Review of Scientific Publications of the Polish Academy of Sciences; The Ossolineum and the Polish Scientific Publishers. Series A: Social Sciences, No. 2. Pp. 35. Series B: Biological Sciences, No. 2. Pp. 35. Series C: Pure and Technical Sciences, No. 2. Pp. 33. (Warsaw: The Ossolineum, 1958.) [229

Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture. Comptes Rendus de Recherches, No. 20 (Septembre, 1958): Travaux du Comité pour l'Étude Scientifique de la Lactation. Pp. 126. (Bruxelles: Institut pour l'Encouragement de la Recherche Scientifique dans l'Industries et l'Agriculture, 1958.) 95 Belgian francs. [229

Deutscher Wetterdienst: Seewetteramt. Einzelveröffentlichungen. Nr. 16: Zur Niederschlagsmessung auf See: Ergebnisse von Vergleichsmessungen auf Feuerschiffen und Benachbarten. Von Dr. H. U. Roll. Pp. 1+15. 1.30 D.M. Nr. 17: Statistik der Meereswellen in der Nordsee. (Auf Grund von Beobachtungen der Bordwetterwarten des Deutschen Wetterdienstes). Bearbeitet von O. Petri. Pp. 1+38. 2.50 D.M. (Hamburg: Deutscher Wetterdienst, 1958.) [229

Publications of the 12th International Congress on Occupational Health held in Helsinki 1–6. 7. 1957. Vol. 1: 32 Reports. Pp. 311. Fmks. 1,000. Vol. 2: 245 Summaries. Pp. 151. Fmks. 600. Vol. 3: 276 Papers, etc. Pp. 622. Fmks. 4,000. (Helsinki: Institute of Occupational Health, 1958.) Price per set 4,500 Fmks.; bound in plastic in one volume, 5,000 Fmks. [229

The Survey of India during War and Early Reconstruction, 1939–1946. By Brigadier Sir Oliver Wheeler. Pp. xii+317+9 plates+3 maps. (Dehra Dun, U.P.: Geodetic and Research Branch, Survey of India, 1955.) Rs. 23. [229

Commonwealth Scientific and Industrial Research Organization, Australia. Division of Fisheries and Oceanography. Technical Paper No. 4: Tasmanian Farm Dams in Relation to Fish Culture. By A. H. Weatherley. Pp. 24. (Melbourne: Commonwealth Scientific and Industrial Research Organization, 1958.) [239

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